CAN TWITTER MAKE MONEY?
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SPECIAL REPORT

MOST INNOVATIVE COMPANIES IN THE WORLD

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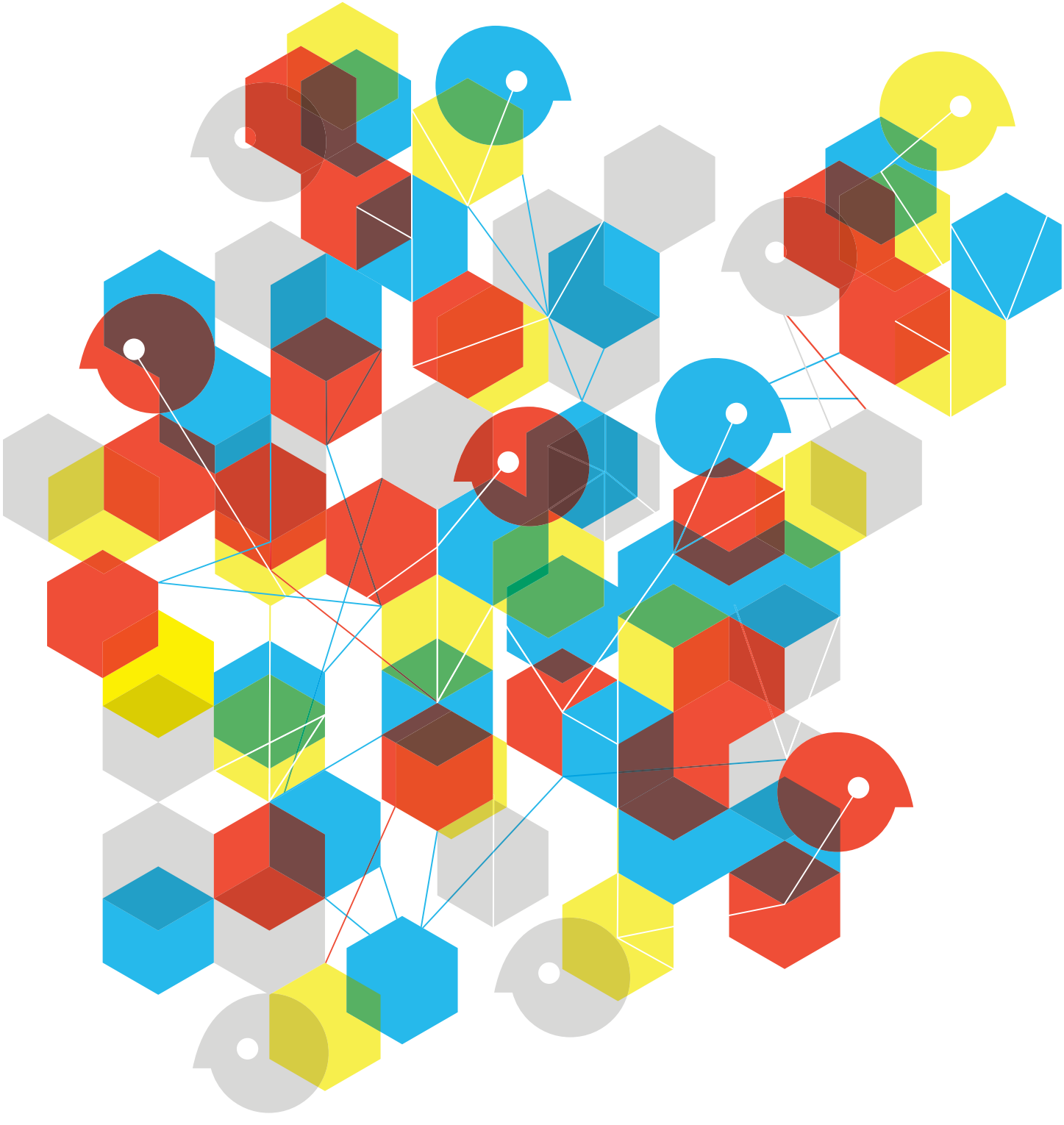
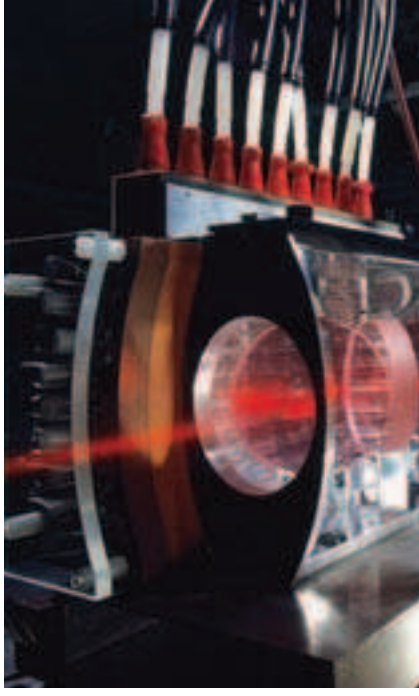


COVER
Photograph by Ian Allen outside IBM's Watson Research Center. IBM is one of the TR50, the most innovative companies of 2010.



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Sick Capital

WHY IT MATTERS THAT VCS WON'T DO THEIR JOBS.

If venture capital is sickly, does it matter? Put another way: would the startups in the TR50, *Technology Review*'s new list of the 50 most innovative companies *(p. 33)*, be more innovative and sustainable, or even different, better ventures altogether, if venture capital were healthier?

Venture capital isn't what it was. Funds launched in 1996 and 1997 saw returns of 80 to 100 percent, according to Cambridge Associates; those launched in 1999 and 2000 lost money. Since then, many have returned less than zero, and only recently has the industry showed signs of life. In "What's Wrong with Venture Capital" *(p. 74)*, James Surowiecki writes, "As Fred Wilson, a principal at Union Square Ventures, bluntly puts it, 'Venture capital funds, as a whole, basically made no money the entire decade.'" What went wrong? The reasons are summarized by Surowiecki (and by Howard Anderson, cofounder of Battery Ventures, in "Good-Bye to Venture Capital," June 2005 and at technologyreview.com).

First, the markets for new technology stocks, the most important means by which VCs recover their investments, are nearly frozen, and the valuations of companies that do enjoy public offerings are no longer irrational. In 2009, just 13 venture-backed companies went public, down from 271 in 1999. Worse, as Anderson wrote, "rational markets value companies at two and a half times their sales at an [IPO]." That's bad for VCs: since most startups fail, a return of 250 percent on those ventures that succeed isn't *that* great, considered over the lifetime of the investment (typically, at least five years). Anderson may be forgiven for having written, "We need a little irrationality to earn a living." VCs once expected that one wonderful success in every 10 of their investments would justify their failures; no longer.

Second, no one buys as much technology as they once did. IT spending by enterprises grew at 15 percent during most of the 1990s but has grown only by single digits for most the last decade. More striking, as Surowiecki points out, "much of the value that new businesses are creating in fields such as social networking is ... 'nonmonetized.'" Users think Facebook and Twitter should be free, and there is no reason to think that VCs' investments in social technologies will be as lucrative as their investments in enterprise software and networking equipment during the 1990s.

Third, there is too much venture capital, but entrepreneurs need less funding. The venture industry now manages about $200 billion, twice what it did in 1998, and invests $20 billion to $30 billion every year; but the cost of launching startups, at least in the software and Internet sectors, has fallen "by at least an order of magnitude," according to Fred Wilson, because of open-source and outsourced software development and the falling price of processing, storage, and bandwidth. In the absence of an irrational market for technology stocks, there's no way for venture capitalists to generate handsome profits on $30 billion of what is, we must remember, called "risk capital."

Does all this matter? Surowiecki writes, "What we care about, after all, is not whether investors get good returns or VCs are well paid. We care about whether new companies are getting started and innovations are being funded."

But the sickliness of venture capital does matter to entrepreneurs, and it should matter to you, too. VCs no longer perform their historical functions: recognizing a few potentially disruptive technologies, finding great entrepreneurs who burn to commercialize those technologies, providing measured seed funding, and worrying startups to profitability. Instead, the partners of the typical fund invest more money, much later, in more companies, selected according to some risk management philosophy.

A well-known Silicon Valley investor (who asked that I not name him, lest he offend his partners) expressed the consequences: "VCs spread themselves over six to 12 portfolio companies, often spending as little as a day a month on each. This is terrible for both entrepreneurs and the country." There's research to back him up: Josh Lerner, a professor at Harvard Business School, has shown that the advice of VCs is an important reason why venture dollars are "three to four times as potent" as corporate R&D in spurring innovation. (On page 12, read why Lerner thinks governments are so bad at encouraging entrepreneurs.)

Past venture capitalists funded the technology companies that became the engines of the world's economic growth: Intel, Microsoft, Genentech, Compaq, Apple, Cisco. But there have been just two really transformative venture-backed companies in the last decade: Facebook and Twitter.

Might Twitter have sooner answered the question that we pose on page 52 ("Can Twitter Earn Money?") had its VCs been more like their predecessors? My unnameable investor told me: "I wish the VCs on the board at Twitter would drop everything else and help Twitter build the solid business that the service so richly deserves. In the past, they would have." Write and tell me what you think at jason.pontin@technologyreview.com. —*Jason Pontin*

MARK OSTOW

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KEEP IT IN THE LAB

A professor of science, technology, and society at Colby College responded to Kevin Bullis's article on the serious attention now being paid by prominent scientists to geoengineering schemes to combat global warming ("The Geoengineering Gambit," January/February 2010).

At MIT's "Engineering a Cooler Earth" symposium last October 30, audience responses to "Should We Try?" were more supportive and robust than those to "Can We Do It?" Of course we cannot and should not do it, since climate engineering is untested and dangerous. The American Meteorological Society's policy statement on geoengineering (also adopted by the American Geophysical Union) recommends more research of an interdisciplinary nature on any proposals to geoengineer climate. It urges coördinated study of the historical, ethical, legal, and social implications of geoengineering, and it calls for the development and analysis of policy options, including restrictions on reckless efforts to manipulate the climate. As I recently told the U.S. House Committee on Science and Technology, support is urgently needed for historical studies of existing environmental treaties, international accords, and efforts to govern new technologies. Any other geoengineering research should be conducted in labs and with computer models, not out of doors.

James Rodger Fleming
Waterville, ME

THE PRICE OF EVERYTHING

Commenters on Bryant Urstadt's article on high-frequency trading ("Trading Shares in Milliseconds," January/February 2010) had a vigorous debate over the legitimacy of the practice. Urstadt's reporting highlighted the ways by which high-frequency traders seek to use technology to exploit opportunities in the market—but also the dangers to markets that some experts feel are introduced in the process.

Tell me exactly what product or service these companies provide? I understand they make money by gambling on being faster than the next guy, but what do they produce that helps America's GDP? … [T]he value of America is in the products and services. Finance is a support function. We need our engineers building things, not moving money.

jjs

Those that have the view that high-frequency trading does nothing for the economy also probably think that equity markets do nothing for the economy and that the whole thing is simply a huge casino. Right .... ? Wrong. Equity markets price capital. In an increasingly automated world, this is the single most productive task humans are capable of engaging in. Said pricing leads to an efficient distribution of capital, which in turn results in a better quality of life in the aggregate. High-frequency traders simply engage in arbitrage: they prevent pricing abnormalities from materializing and therefore make pricing more efficient.

GreenPlease

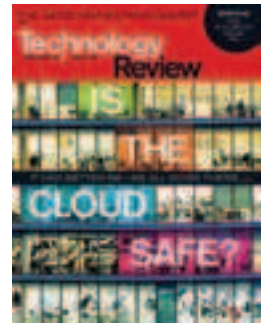
Why do I get the feeling that you were spinning exactly the same line about CDOs just a few years ago? And that in a few years' time you'll be saying just the same about the next brilliant idea to emerge from Wall Street after HFT has caused another financial crisis, impoverishing millions of people (except, of course, the traders)?

The most productive task in the world? The best paid, possibly.

chrisjmiller

My experience is that the financial markets work very well for small investors. I'm an "old-fashioned" buy-and-hold investor who makes small (~$1000) purchases. Commissions are now very small ($0 to $5), trades are executed instantaneously, and, as mentioned in the article, the spreads are only a few pennies per share. Even in the depths of the market turmoil, everything functioned normally and I was able to execute trades. It is hard to imagine that HFT doesn't contribute to the proper functioning of markets. … The real problems lie with investor psychology. Successful investing is about as interesting as watching paint dry. Investors, however, try to make it into a night at the casino.

hpwarren



January/February '10

LOST IN SPACE

A reader wrote in support of one of the conclusions of the Augustine Committee's report on space exploration, reviewed by Jeff Foust ("The Future of Human Spaceflight," January/February 2010).

Given the challenges of climate change in the medium run and a new ice age in the long run, one cannot but agree with the conclusion of the Augustine Committee that "the ultimate goal of human exploration is to chart a path for human expansion into the solar system." But NASA seems to be lost in space at present. Even keeping the International Space Station (ISS) in orbit beyond 2015 is now in question. As Jeff Foust put it, if people are going to live and work in space, the ISS is the ideal laboratory to test technology and human performance under long-term conditions. In addition, it may in time serve as a staging station for bases in the inner solar system—the moon, Mars, and the asteroid belt. In short, it is clear that the ISS must not be "deorbited" for lack of funds soon after its completion in 2011. There is an urgent need for an international space agency that would pool resources of all space-faring nations toward the fundamental goal of human

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expansion into space. That goal must not be put in question. Ever.

Ranko Bon
Motovun, Croatia

CATCH ME A CATCH

Emily Gould's article review of Match.com ("True Match," January/February 2010) prompted one online-dating veteran to write.

As a 52-year-old widower who has used the likes of Match.com, eHarmony.com, and Chemistry.com for the better part of eight years, I found the article very unbalanced. Ironically, Match.com promotes itself as much more of a simple "clearinghouse" than the other two—an online version of the print media's personals section, but with photos and long self-written narratives. It is no more Match.com's fault that it didn't find the author (or her friend) a decent date than it is an online brokerage firm's fault that there aren't any A+ funds yielding more than 1 percent APR. And I must ask how the author can lament that her friend's date didn't ask her a single question at their first lunch—didn't she have a phone conversation with him ahead of time that would probably have highlighted this habit, or did she just assume that any guy the computer found would be "Mr. Wonderful"?

Henry Fiorentini
Lincolnshire, IL

CLARIFICATION: "The Geoengineering Gambit" (January/February 2010) says that Himalayan glaciers could disappear within 25 years, a claim based on information published in the most recent report from the Intergovernmental Panel on Climate Change (IPCC). Since the report was published, it's become clear that the glaciers won't melt by then. The estimate could be off by 300 years or more, according to some glaciologists.

The IPCC, which is known for its use of peer-reviewed literature and multiple layers of expert review, in this case cited not scholarly work but, instead, a magazine article. After our article was published, it issued a statement declaring that the claim was based on "poorly substantiated evidence" and that "the clear and well-established standards of evidence, required by the IPCC procedures, were not applied properly."

A letter written to the journal Science *by noted glaciologists, published after our article, says: "The claim that Himalayan glaciers may disappear by 2035 requires a 25-fold greater loss rate from 1999 to 2035 than that estimated for 1960 to 1999. It conflicts with knowledge of glacier-climate relationships and is wrong. Nevertheless, it has captured the global imagination and has been repeated in good faith."*

We regret that we published what now appears to be incorrect information about the Himalayan glaciers.

The main point of the feature, however, isn't affected by this mistake. Scientists remain concerned enough about rapid climate change to recommend studying geoengineering methods for rapidly cooling the earth. The disappearance of the Himalayan glaciers was only one reason, and indeed not even the main reason, cited by these scientists.

Q&A

BILL GROSS

Can a veteran dot-com investor make solar power as cheap as coal?

Bill Gross was famous during the Internet boom as the founder of Idealab, an "incubator" that hatched more than 75 companies. His best-known investment was GoTo.com, which created an online marketplace where advertisers bid for primacy in the results of Web searches—the innovation, now called "keyword advertising," that made Google wildly rich (with the all-important tweak that sponsored and algorithmically derived results should be clearly separated). GoTo.com (which became Overture Services) was sold to Yahoo for $1.6 billion in 2003.

Of course, Gross (and Idealab) never really went away. Among Gross's recent investments is eSolar, a TR50 startup of which he is chairman. The company hopes that with its technology, solar thermal energy—heat and electricity generated from sunlight using mirrors—will cost no more than coal-generated power. Jason Pontin, *Technology Review*'s editor in chief, met with Gross at the 2010 annual meeting of the World Economic Forum in Davos, where eSolar was honored as a Technology Pioneer.

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PAGE 39

***TR:* Why did eSolar choose solar thermal power, which has been little implemented beyond a handful of utility plants?**

Gross: We want to compete with coal. We looked at all of the renewable technologies that can be deployed at scale, and they were all variations of solar thermal. It has the capacity for scale because all the materials are readily available: there's enough steel and glass to power the planet with solar thermal. Solar thermal's potential has, so far, been theoretical, but we're going to try to make it a reality.

But how are you different from established solar thermal companies, some of which are almost 20 years old?

Abengoa [Solar, a Spanish company founded in 1984] has made many solar towers, and there have been others deployed at scale. But there's been no disruption [of fossil-fuel-generated power]. The problem is, there's been too much civil construction: if you want solar thermal to disrupt the energy market, you need its parts to be mass-produced like an automobile. A 200-meter-tall solar tower [upon which the mirrors are focused] is a skyscraper, and it takes a year to build. So we decided to go with small towers and small mirrors, all of which can be prefabricated in a factory. We have a two-piece tower that gets erected in one day. All of our mirrors, all of our frames, fit in a shipping container, which means you can make them in China and ship them anywhere. When your stuff is smaller than a container, you switch from a few big moving elements to hundreds of thousands of small moving elements. That's the disruptive switch we've made—and that posed a new challenge.

You're referring, I think, to the software eSolar developed that allows thousands of mirrors to more precisely reflect sunlight back to a tower.

The software is the differentiation at eSolar. It's challenging because all those mirrors don't move the same way. Every mirror is moving slightly differently, bisecting the angle between the tower and the sun all day long. Other solar thermal players have to survey everything very accurately. They figure out where they think the sun should be, where the tower is, and try to bisect the angle of the mirrors mechanically. We are the only ones who have ever actually tracked the exiting beam [of sunlight] from the mirror. That's hard to do with software, and we've patented it. But the reward is that when we place the mirrors, they're not surveyed at all: we open our shipping container, we unfold our stuff, and we place it in the ground. The guys can be drunk when they place the rows; it really doesn't matter. Our tolerance is plus or minus a foot.

That's how you'll make your solar thermal power cheaper than existing solar thermal?

Processing power is cheap, and in energy, it's the only thing that's getting cheaper. All other commodities, long term, are going to go up in price. That's how we're going to compete with fossil fuels: just pour software at the problem.

What's wrong with photovoltaic power?

You'll never be able to beat coal with photovoltaic technology. The PV cell is not the only expensive part. First Solar, a great PV manufacturer, is down to, like, 90 cents a watt for the actual panel. If they drive that down to zero, it still doesn't matter, because the cost of skilled labor to install the PV and its low capacity factor will result in price minima [the prices beneath which products or services cannot fall, even as new efficiencies are brought to bear]. And they're *not* going to get to zero, because there are expensive materials in there. For us, we will drive the price of power closer and closer to the cost of the glass, but because of our modular design, because we have prefabrication, because we're running at triple to quadruple the efficiency of PV, they can never touch our price.

Idealab has mostly invested in Internet ventures like GoTo.com. Why eSolar?

I think that maybe eSolar is as disruptive an idea as GoTo. And I would like to think that as GoTo was a $100 billion opportunity for Google, this will turn into a $100 billion opportunity, too. TR

Photograph by DARRIN VANSELOW

Bill Gross and Editor in Chief Jason Pontin talked with each other in Davos, Switzerland, at the annual meeting of the World Economic Forum. It snowed.

NOTEBOOKS
Expert opinion

STARTUPS

Publicly Funding Entrepreneurship

WE NEED TO TAKE POLITICS OUT OF GOVERNMENT EFFORTS TO SPUR INNOVATION, SAYS JOSH LERNER.

Literally thousands of government programs worldwide have tried to boost innovative new ventures in recent decades. While some—such as those in Israel and Singapore—have dramatically encouraged entrepreneurial and venture activity, many more have been abject failures. The same critical mistakes have been made again and again, most recently in efforts to boost entrepreneurial innovation in clean tech.

One major problem is that funds end up getting distributed in ways that have less to do with the needs of high-potential ventures or society generally than with the whims of the powerful and well-connected. From the empty Bio-Valley site in Malaysia to the many U.S. Small Business Innovation Research grants won by DC-area firms that produce few real innovations, the pattern is depressingly familiar. Successful programs, by contrast, have well-defined investment processes and limit the danger of political influence by establishing independent administrative bodies.

Faced with a clean-tech funding bonanza in the stimulus bill, entrepreneurs have responded the old-fashioned way: by hiring lobbyists. The big winner of the Department of Energy's battery funding orgy, A123 Systems *(see the TR50, p. 33)*, spent about a million dollars on Washington representatives from 2007 through early 2009. A partner at New Enterprise Associates suggested last March that at least half of its 25 clean-tech firms had hired lobbyists.

The only sure way to prevent political and other pressures from distorting public efforts to boost innovation is to look carefully at which firms private investors think are viable. By focusing on supporting firms that have raised matching funds, public officials can boost innovative entrepreneurs far more successfully.

Yet many recent efforts on behalf of clean-tech firms have shown a willful disregard for market signals. Consider Massachusetts's support for panel maker Evergreen Solar. As its stock price has tumbled from almost $19 in late 2007 to under $1.50 today, the state has continued to fund the firm, in apparent violation of its own spending limits. The crucial consideration in these decisions seems to be not the potential for innovation but, rather, the PR nightmare that could result if the company failed.

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High-potential ventures do not exist in a vacuum. And the Japanese government's unsuccessful efforts to boost entrepreneurs over the past 15 years are evidence enough that without a suitable environment, failure is certain. The United States should focus on ensuring that the overall economic environment is attractive to entrepreneurs (for example, through low marginal tax rates on long-term capital gains), that subsidized firms and venture funds are able to raise matching funds from private investors, and that government programs to promote innovation are implemented in a thoughtful and transparent manner. TR

JOSH LERNER IS A PROFESSOR OF INVESTMENT BANKING AT HARVARD BUSINESS SCHOOL. HIS LATEST BOOK IS *BOULEVARD OF BROKEN DREAMS: WHY PUBLIC EFFORTS TO BOOST ENTREPRENEURSHIP AND VENTURE CAPITAL HAVE FAILED—AND WHAT TO DO ABOUT IT.*

VENTURE CAPITAL

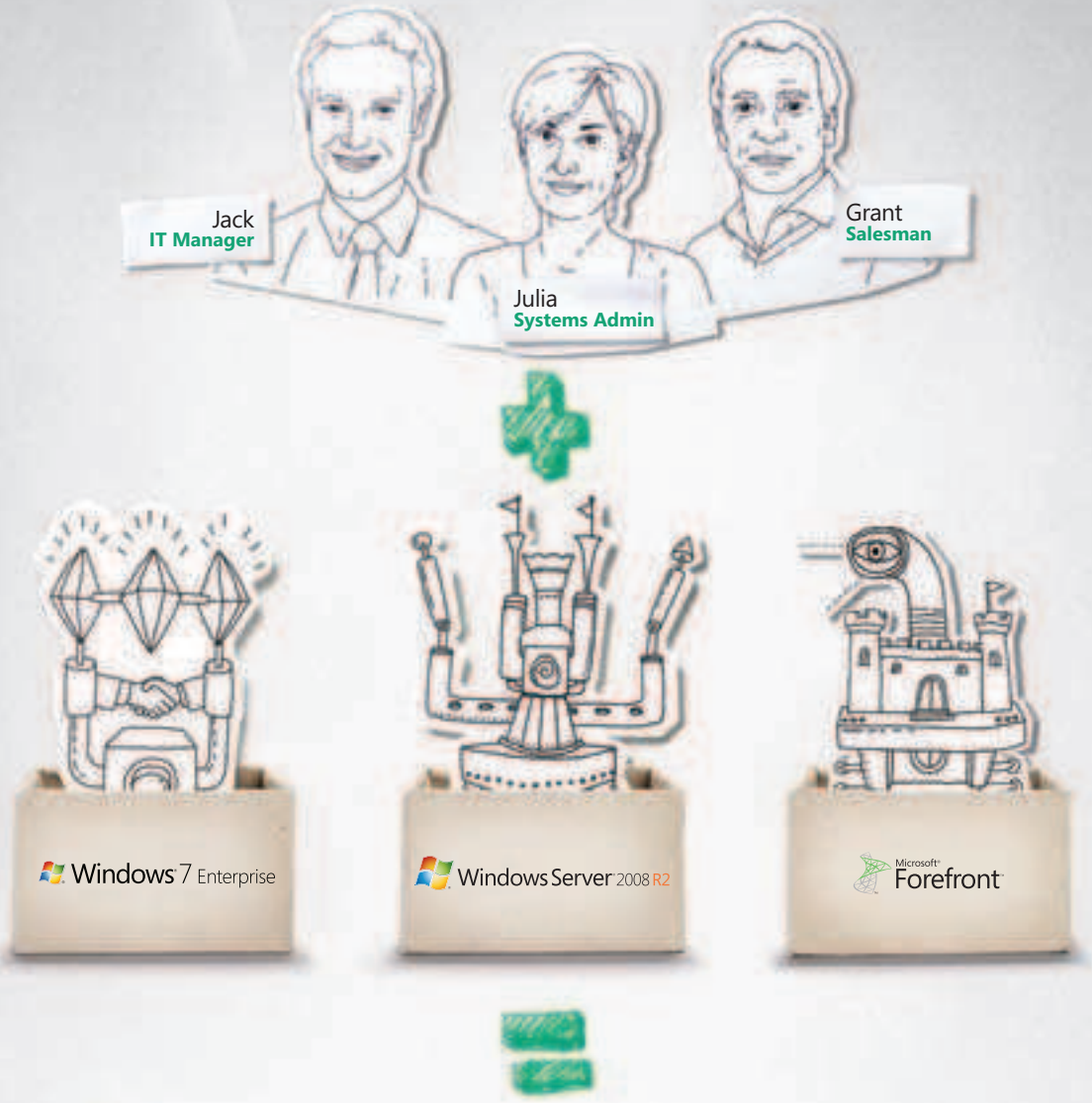
The Pace of Innovation Never Falters

STEVE JURVETSON ASSERTS THAT INNOVATION AND ENTREPRENEURSHIP ARE THRIVING.

Innovation is critical to economic growth and progress, and yet it seems so random. But if we step back, a pattern emerges. The pace of innovation is accelerating and is *exogenous to the economy*. At Draper Fisher Jurvetson, we see that

NICK REDDY/HOFF

Microsoft



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pattern in the diversity and quality of the entrepreneurial ideas coming into our offices. Scientists do not think more slowly during recessions. Startup proposals seem *better* during downturns.

For a model of the pace of innovation, consider Moore's Law—the annual doubling of computer power or data storage capacity. As Ray Kurzweil has plotted, these increased exponentially from 1890 (with punch-card computing) to 2010, across countless technologies and human dramas. Most recently, we have seen Moore's Law revolutionize the life sciences, from genomics to medical imaging, and work its magic in ever bigger and more diverse industries.

Technology's nonlinear pace of progress has created a juggernaut of perpetual market disruption, spawning wave after wave of opportunities for new companies. Without disruption, entrepreneurs, and VCs like me, would not exist.

During previous recessions, false oracles declared innovation dead because they did not see any in mature industries like enterprise software. Predictable and stable industries resist new entrants. Entrepreneurs and VCs have to follow disruption across markets. Many of the TR50 *(p. 33)* will no doubt lead the way.

Here are two foundational innovations to ponder that offer a variety of disruptive opportunities in coming years.

First, 2010 will be the year of the first scalable quantum computer. (I am an investor in D-Wave, a startup building a commercial quantum computer: see "Riding D-Wave," May/June 2008.) If it follows "Rose's Law" (named after Geordie Rose, a cofounder of D-Wave), annually doubling qubits for the next 10 years, it will handily outperform all computers on the planet combined.

It will also be the year of the first synthetic life form: 100 percent of its DNA will be made from scratch, from beakers of chemicals. This will introduce a new era of intelligent design in biology, in which technologists will write the code of life as if it were a computer program. Energy and chemical giants will experience the whiplash of Moore's Law, as biotech companies create and test billions of novel microbial workhorses every day.

I don't accept the gloomy assessment captured by James Surowiecki *(see "What's Wrong with Venture Capital?" p. 74)*. We haven't seen anything yet. TR

STEVE JURVETSON IS MANAGING DIRECTOR OF DRAPER FISHER JURVETSON, A VENTURE CAPITAL FIRM IN MENLO PARK, CA.

GOVERNMENT

Transforming Energy

ARUN MAJUMDAR EXPLAINS HOW A GOVERNMENT FUNDING AGENCY AIMS TO SOLVE THE ENERGY PROBLEM.

Radical innovation can alter the landscape of an entire industry. That's the goal of the newly formed Advanced Research Projects Agency for Energy, part of the U.S. Department of Energy. Modeled after the Defense Advanced Research Projects Agency (DARPA), ARPA-E was funded for the first time in last year's American Recovery and Reinvestment Act to pursue transformational solutions to the energy problem.

ARPA-E was originally proposed in a National Academies report, *Rising Above the Gathering Storm*. Energy Secretary Steven Chu—then director of the Lawrence Berkeley National Laboratory—was part of the committee that proposed to create a nimble, creative agency.

After President Obama announced this effort in April, we received nearly 3,700 submissions. Five hundred expert reviewers put in nearly 8,700 hours to choose 37 projects—1 percent of the submissions.

The projects were selected through the most rigorous peer review process the DOE has engaged in. Secretary Chu sent a letter to the presidents of major

research universities and the heads of the engineering societies asking them to name the best scientists and engineers in the country. We asked these people to serve as reviewers, arguing simply that this work was part of their patriotic duty to our country and the world.

We are now hiring top *practicing* scientists and engineers to serve as program directors. In addition to guiding the projects, they will seek out additional areas that are ripe for breakthroughs.

The 37 projects we're funding span the spectrum—renewable energy, energy storage, industrial and building efficiency, petroleum-free vehicles, carbon capture *(for some companies addressing these issues, see the TR50, p. 33)*. The ideas are potentially revolutionary. They are risky, and many of them will fail. But this is high-risk, high-reward research: if one or two ideas lead to transformative technologies, it will be among the best investments we've ever made.

We are determined to attract the best and brightest minds to solving the energy problem. This is truly the scientific and engineering challenge of our time. Scientists and engineers have come to our nation's aid in past times of need, and it is time for them to do so again.

The stakes could not be higher. Great ideas have transformed our world before. But new great ideas on energy might do more than just change our world—they might help save it. TR

ARUN MAJUMDAR WAS APPOINTED DIRECTOR OF ARPA-E IN OCTOBER 2009.

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Fueling the 21st Century

Recently, the U.S. Department of Energy announced more than $600 million in grants for 15 projects that are developing the next generation of biofuels. These grants demonstrate the Obama administration's interest in rapidly moving biofuels—alternatives to corn-based ethanol—through the pilot and demonstration stages and into commercial production.

Next Generation Biofuels

INP BioEnergy, a joint venture of Ineos Bio and New Planet Energy, was selected to receive a $50 million grant to develop a commercial demonstration plant for a new biowaste gasification-to-ethanol process. In this system, various mixed organic feedstocks, such as agricultural waste, yard waste, and construction debris, are gasified, using controlled temperatures and environments to produce synthesis gas—known as syngas—made primarily of carbon monoxide and hydrogen. Heat from the process produces steam that can spin a turbine to generate electricity, while the cooled syngas is fed to a specially developed mixture of bacteria to ferment the syngas and produce ethanol. David King, president of INP BioEnergy, explains that the gasification process also destroys organic pollutants.

A pilot plant has been running for the past six years in Arkansas. The new funding will allow the partnership to build a larger demonstration plant; the company is currently looking at Vero Beach, Florida as the potential location.

Pith and Peel Energy

Florida's wealth of agricultural waste has proven attractive to other biofuel ventures as well. The state produces about 90 percent of the country's orange and grapefruit juice, and its citrus industry generates about 5 million tons a year of pith and peel. That staggering volume inspired David Stewart, president of Boca Raton-based Citrus Energy.

According to Stewart, "most biofuels research had been done on lignocellulosic feedstock, such as trees or corn, but citrus … has no lignan in it, it has pectin." So company engineers developed a cocktail of enzymes that can break down citrus, then focused on reducing the quantity of enzymes in the process to reduce the cost. Citrus Energy is now raising funds for a pilot plant.

Bagasse to Ethanol

Along with citrus, Florida's agricultural sector is known for sugarcane. Florida Crystals, which produces 6 million tons of sugarcane a year, has traditionally used bagasse as a feedstock for the company's electricity production. (Bagasse is the woody waste that remains after juice is extracted from sugarcane.) In recent years, however, Florida Crystals has been evaluating a process to convert bagasse to ethanol instead, which could be a more efficient and valuable use for it.

In partnership with Florida International University (FIU), the firm has developed an on-site pilot plant at its Palm Beach County facilities to convert bagasse into ethanol. Sugarcane bagasse is slightly different from other woody feedstocks such as switchgrass, according to George Philippidis, FIU's energy director. Researchers have developed a proprietary process that uses moderate heat and low concentrations of chemicals to soften the bagasse before enzymes are introduced to break the long sugar chains into simple sugars.

"The goal has been to minimize the capital costs by using off-the-shelf equipment, minimize environmental impacts [from the chemicals needed to break down the pulp], and minimize energy consumption," says Stephen Clarke, direction of industrial R&D for Florida Crystals. Clarke reports that by late 2010 the project will evaluate expanding to a larger facility.

To make cellulosic ethanol commercially viable, hurdles of cost, efficiency, and environmental impact must still be cleared. Nonetheless, as Anthony Martino puts it, "There's a tremendous amount of hope for cellulosic ethanol, as there's a tremendous amount of resources in the country."

TO MARKET

AASHITH SHETTY

TRANSPORTATION

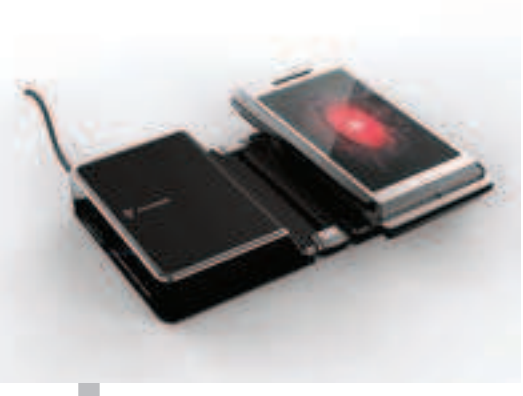
HYBRID MOPED

THE ET-120 is billed as the first commercial hybrid two-wheeled vehicle. Designed for the crowded streets and limited budgets of India, it won't be setting any speed records (it tops out at 65 kilometers per hour), but the price is right at less than $1,000. Electrical energy is stored in lead-acid batteries, and the bike gets 120 kilometers per liter of gas, compared with about 25 to 75 kilometers per liter for conventional mopeds.

Product: ET-120 motorcycle
Cost: Approximately $800
Availability: Mid-2010
Source: www.ekovehicle.com
Companies: Eko Vehicles, Emerging Vehicle Technologies

MOBILE DEVICES

TECH FOR TRAVELERS



Wireless Power

THE POWERMAT Portable is intended for travelers who are tired of lugging around a collection of chargers for mobile devices. Place any device on the mat, and it uses induction to deliver a wireless charge; the power flows to small receivers that can be fitted to most handheld gadgets. The Powermat is powered by an AC adapter, but a built-in lithium-ion battery allows charging when you can't find a wall socket.

Product: Powermat Portable **Cost:** $100 **Availability:** Fall 2010 **Source:** www.powermat.com **Company:** Powermat

FASTER PORTABLE DRIVE

WITH USB 3.0, the next generation of the popular USB standard for connecting peripherals, this portable hard drive can transfer data up to three times as fast as USB 2.0 drives can. The hard drive has 500 gigabytes of storage capacity and comes with an adapter card for laptops not equipped with built-in USB 3.0 ports. (The new ports are compatible with USB 2.0 devices and cables, but USB 2.0 cables cannot be used with USB 3.0 devices.)

Product: BlackArmor PS110 3.0 **Cost:** $180 **Availability:** Now **Source:** www.seagate.com **Company:** Seagate

POCKET PROJECTOR

THE MPRO150 is designed for those times when the screen of a laptop or iPhone just isn't big enough. The device uses liquid-crystal-on-silicon technology to display images projected with a super-bright LED. With a cable, it can show presentations and videos directly from laptops, iPods, and iPhones. It can also play files preloaded into either a memory card or the projector's one-gigabyte built-in memory.

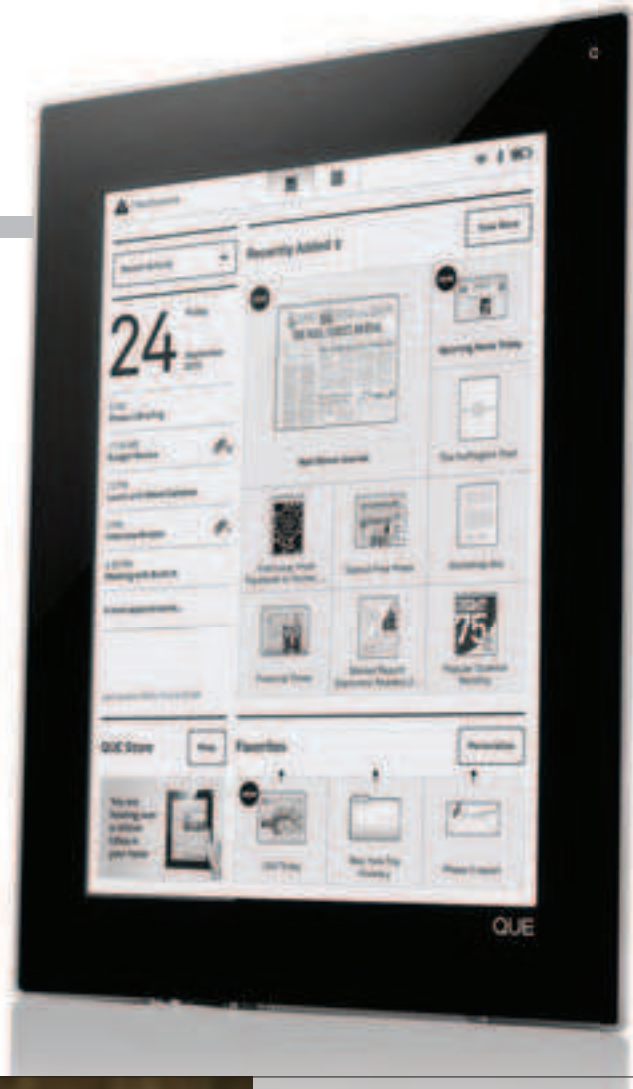
Product: MPro150 **Cost:** $395 **Availability:** Now **Source:** www.shop3m.com **Company:** 3M

COURTESY OF POWERMAT (POWERMAT); JOSHUA SCOTT (USB DRIVE); COURTESY OF 3M (PROJECTOR)

PLASTIC PAPER

AIMED AT business users, the Que e-reader uses a 266.7-millimeter display from E Ink, based on the same sort of technology used in the Kindle. But unlike other e-reader displays, which are controlled with silicon transistors on a glass backing, it uses organic transistors deposited on plastic. This makes for a lighter, tougher device.

Product: Que
Cost: $650 to $800
Availability: April 2010
Source: www.que.com
Company: Plastic Logic



TV on the Go

THIS TV receiver takes advantage of a new mobile TV standard, now beginning to roll out across the United States, that allows good reception of digital TV broadcasts even in a moving vehicle. Using Wi-Fi, the Tivit retransmits the video so it can be watched on a smart phone, netbook, or iPhone.

Product: Tivit **Cost:** $90 to $120 **Availability:** March 2010
Source: www.valups.com **Company:** Valups

DIGITAL LEASH

TRAVELERS WHO worry about leaving their phone in a hotel room or airport will like this small Bluetooth device designed to be worn on a keychain. The Zomm monitors the signal strength of a Bluetooth connection to your phone and sounds an alert if you get more than a few yards away. It can also be used as a speakerphone and as a panic button to call 911.

Product: Zomm **Cost:** $80 **Availability:** Summer 2010
Source: zomm.com **Company:** Zomm

For more To Market items, take a snapshot of this code with your smart phone using software available at www.neoreader.com.

COURTESY OF PLASTIC LOGIC (QUE); COURTESY OF VALUPS (TV); JOSHUA SCOTT (ZOMM)

AUGMENTED REALITY

TOY DRONE

INSTEAD OF using a traditional remote, this flying toy can be controlled by any iPod Touch or iPhone running special software. A camera communicates with the controller over a Wi-Fi connection, delivering a pilot's-eye view to the user's screen. Graphics representing enemy planes can be overlaid on this view with augmented-reality technology, and the AR Drone can dogfight with them. Thanks to all the onboard processor power available, it can take advantage of technology that keeps it much more stable in flight than similar toys. As a second camera scans the ground below, the Drone automatically adjusts its engines to keep it flying level or hovering.

Product: AR Drone **Cost:** Not yet determined **Availability:** 2010 **Source:** ardrone.parrot.com **Company:** Parrot

ENERGY

Hydrogen on Demand

SUPPLY-CHAIN challenges have kept the hydrogen economy from becoming a reality, but the Hydrofill refueling station bypasses those problems by letting users make their own fuel. The desktop-sized unit, which can be powered from an AC adapter or an optional solar panel, electrolyzes water to make hydrogen gas. The gas is stored as a solid in metal hydride cartridges, which take an hour to fill; the cartridges can then be used in a handheld fuel-cell recharger that supplies power to portable electronics.

Product: Hydrofill **Cost:** $500
Availability: 2010
Source: www.horizonfuelcell.com
Company: Horizon Fuel Cell Technologies

RADAR

SPEED SENSOR

THE BULKY horn antenna of a traditional radar gun has been compressed down to a square panel about 40 millimeters on a side. Intended for athletes and coaches looking to improve performance, the Pocket Radar uses Doppler radar to measure the speed of an object to within 1.6 kilometers per hour.

Product: Pocket Radar **Cost:** $250
Availability: Spring 2010 **Source:** pocketradar.com
Company: Pocket Radar

COURTESY OF PARROT (DRONE); COURTESY OF HYDROGEN FUEL CELL TECHNOLOGIES (HYDROGEN); JOSHUA SCOTT (RADAR)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BIOMEDICINE

BIONIC FINGER

PATIENTS WHO have lost one or more fingers can now replace their missing digits with powered artificial fingers. While those who have lost an entire hand have been able to use motorized prostheses for years, the small volume of an artificial finger made it difficult to cram in the required electronic and mechanical components. With a miniaturized motor and gearbox at the base of the finger, each ProDigit can be individually controlled using myoelectric impulses.

Product: ProDigit **Cost:** Not available
Availability: Now
Source: www.touchbionics.com
Company: Touch Bionics

MATERIALS

GRAPHIC GRAPHENE

THIS CONDUCTIVE INK is one of the first products on the market to incorporate graphene, a sheet of carbon just one atom thick. Applying the ink with standard techniques can print wiring for RFID antennas, keypads, and display backplanes directly onto paper or cardboard stock. Unlike metallic conductive inks, the graphene ink does not have to be heated after printing.

Product: Vor-ink **Cost:** Not disclosed **Availability:** Now
Source: www.vorbeck.com **Company:** Vorbeck Materials

JOSHUA SCOTT (FINGER); COURTESY OF VORBECK MATERIALS (INK)


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IS YOUR
MEDICAL HISTORY
DELIVERED
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Inventing across Borders

MAPPING INTERNATIONAL COLLABORATION IN R&D

Talk of globalization often focuses on manufacturing, but the map at right shows that the creation of ideas and products is just as much an international affair. A growing number of applications filed under the international Patent Coöperation Treaty (PCT) have authors located in two or more countries. Each line in the map represents one of these collaborations between 2004 and 2006, revealing the complex architecture of global innovation networks.

Smaller countries that need to tap into bigger markets or the research infrastructure of their wealthier counterparts tend to participate heavily in international collaboration. Nearly half of Switzerland's applications, for instance, involve a coauthor abroad; for Thailand, an export-dependent emerging nation, it's three-quarters. Levels of international collaboration vary more among larger countries. Japan and Korea—whether because of geography, language, or culture—participate less in international coinvention than any other major patenters. The United States is the largest collaborator by volume, making connections with nearly every country on earth. *—Matt Mahoney*

THE AMERICAS

Although its ratio of international collaboration is relatively low, the U.S. dominates in sheer volume and global reach.

MAP LEGEND

Lines
PCT applications with coauthor located abroad, 2004–2006

- 1–25
- 26–50
- 51–100
- 101–200
- 201–400
- 401–800
- 801–1,600
- 1,601 or more

Country color
Percentage of PCT applications with coauthor located abroad

- N./A.
- 0%–9%
- 10%–19%
- 20%–29%
- 30%–49%
- 50%–74%
- 75%–100%

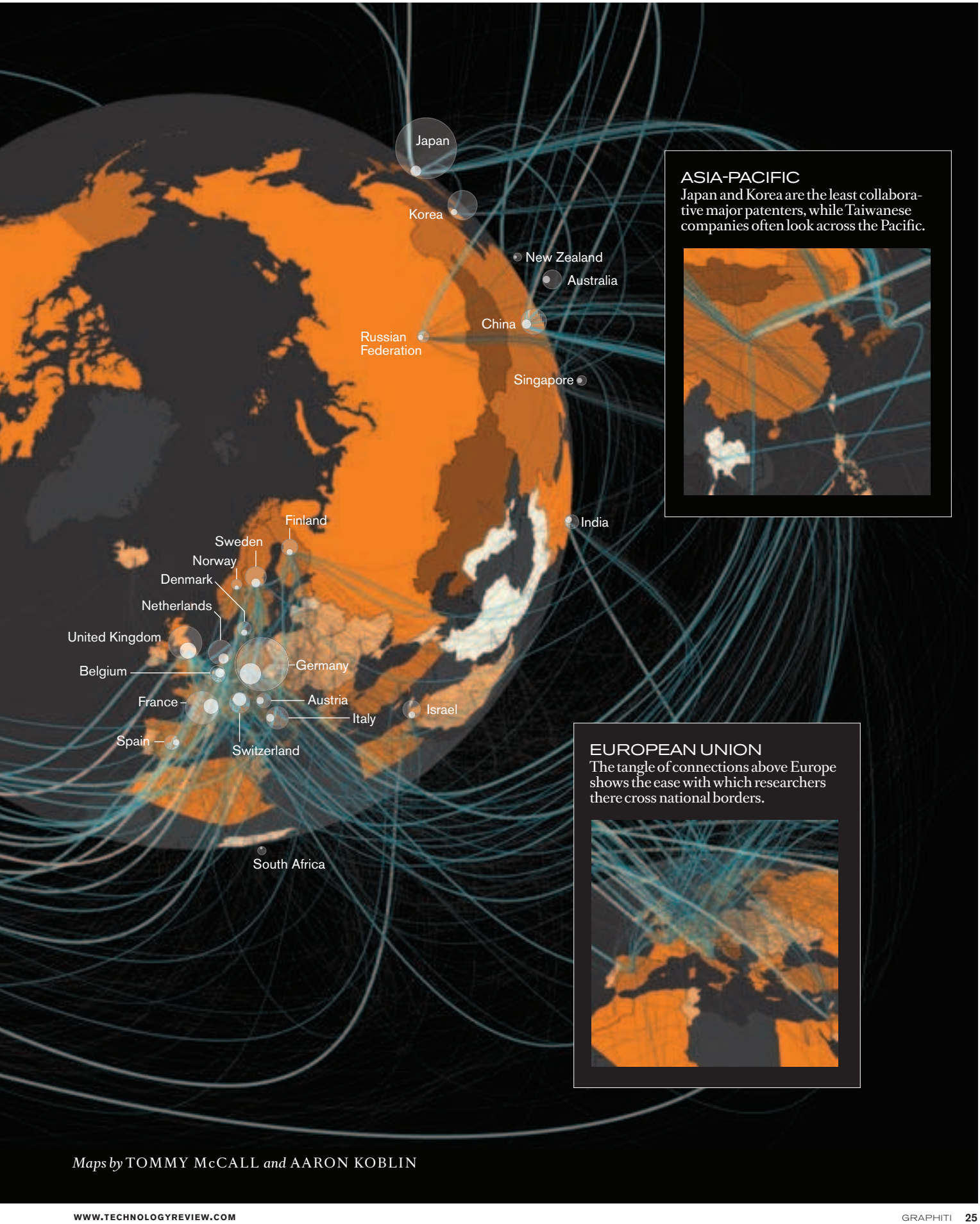
Bubble size
PCT applications authored by top 25 producers

- 150,000
- 100,000
- 50,000
- 25,000
- 10,000
- 1,000

Total patents

Patents with a foreign coauthor

Source: Organisation for Economic Cooperation and Development Patent Database



ASIA-PACIFIC

Japan and Korea are the least collaborative major patenters, while Taiwanese companies often look across the Pacific.

EUROPEAN UNION

The tangle of connections above Europe shows the ease with which researchers there cross national borders.

Maps by TOMMY McCALL *and* AARON KOBLIN

The first laser, demonstrated by Theodore Maiman at the Hughes Research Laboratories, was a ruby crystal rod with mirrored ends, resting in the center of a coiled quartz flash tube. The tube lamp flashed an intense white light, which energized chromium atoms in the ruby. As the atoms lost energy, released photons bounced between the mirrors, stimulating more atoms, before finally escaping out of one end of the rod in short pulses of red light. Shortly after its demonstration, Bell Labs researchers invented the gas laser (right, with Ali Javan, one of the inventors). The first gas laser used an electric current to excite helium and neon atoms, producing a continuous beam of light.

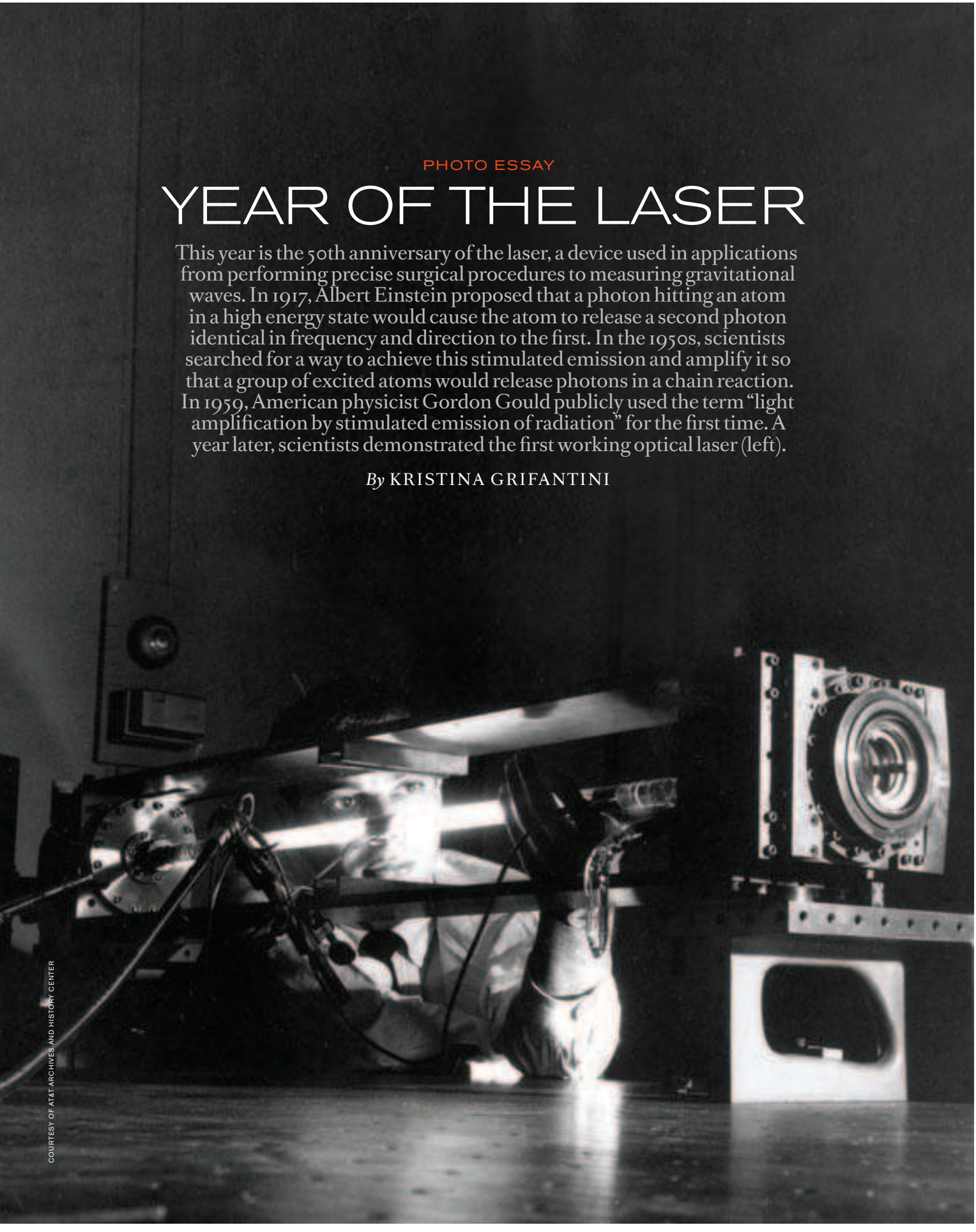
HRL LABORATORIES

PHOTO ESSAY

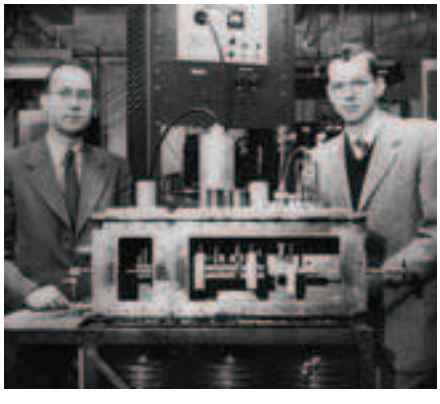
YEAR OF THE LASER

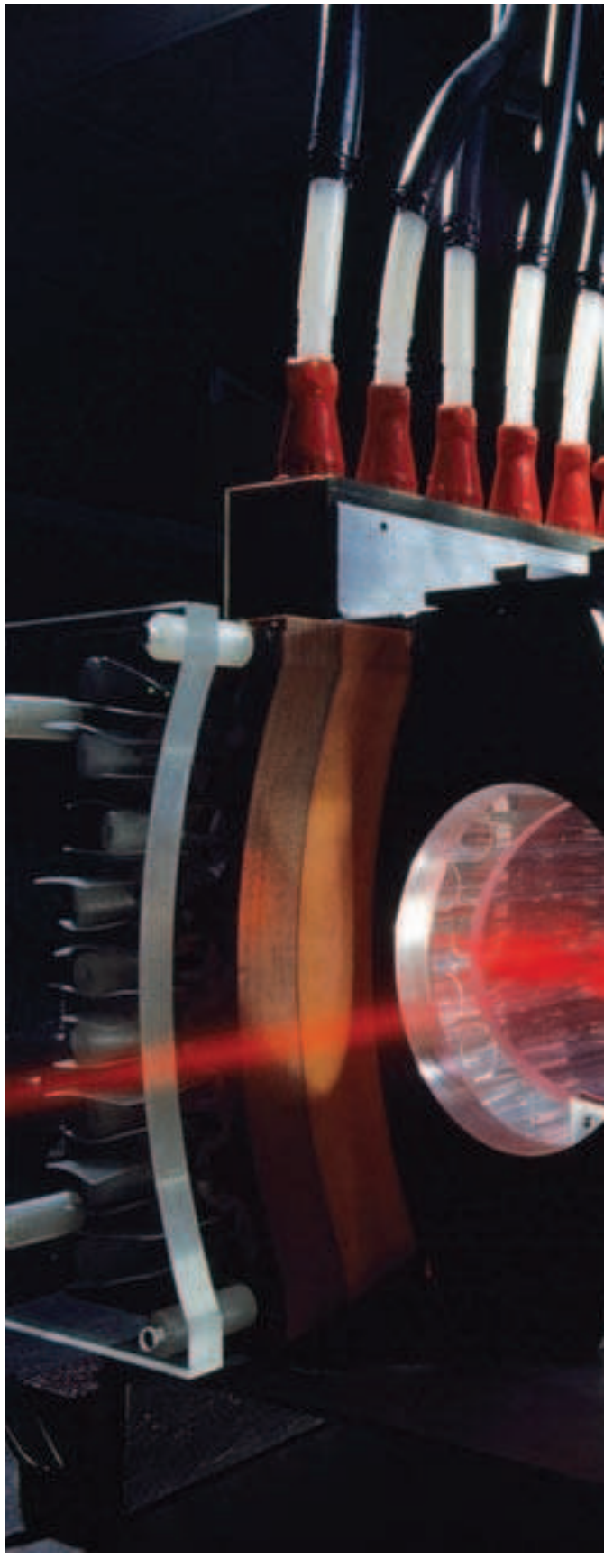
This year is the 50th anniversary of the laser, a device used in applications from performing precise surgical procedures to measuring gravitational waves. In 1917, Albert Einstein proposed that a photon hitting an atom in a high energy state would cause the atom to release a second photon identical in frequency and direction to the first. In the 1950s, scientists searched for a way to achieve this stimulated emission and amplify it so that a group of excited atoms would release photons in a chain reaction. In 1959, American physicist Gordon Gould publicly used the term "light amplification by stimulated emission of radiation" for the first time. A year later, scientists demonstrated the first working optical laser (left).

By KRISTINA GRIFANTINI



COURTESY OF AT&T ARCHIVES AND HISTORY CENTER

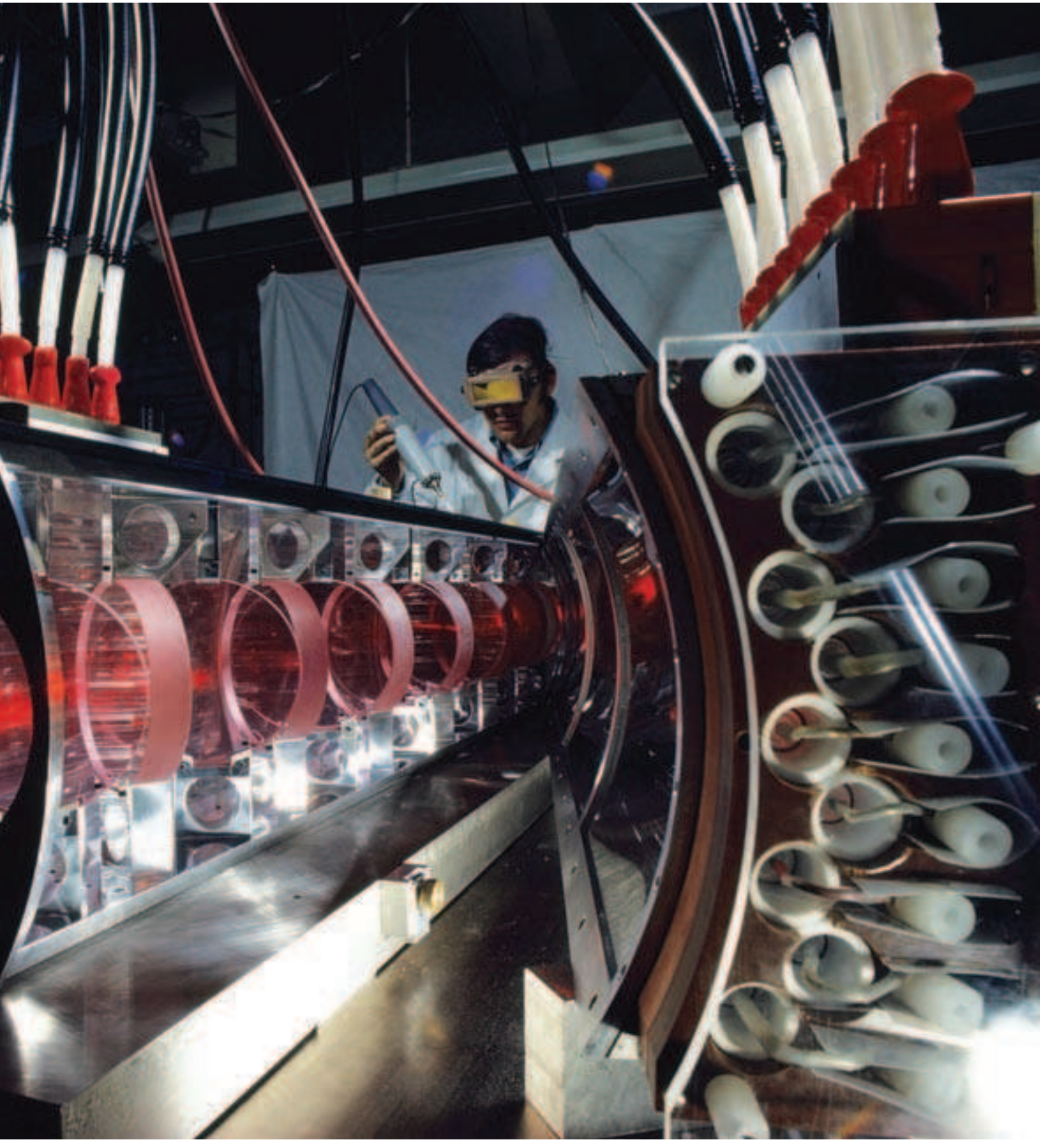




BETTMANN/CORBIS (TOWNES MASER); NASA/JPL (HYDROGEN MASER); JAMES P. BLAIR/NATIONAL GEOGRAPHIC/GETTY IMAGES (ROCHESTER)

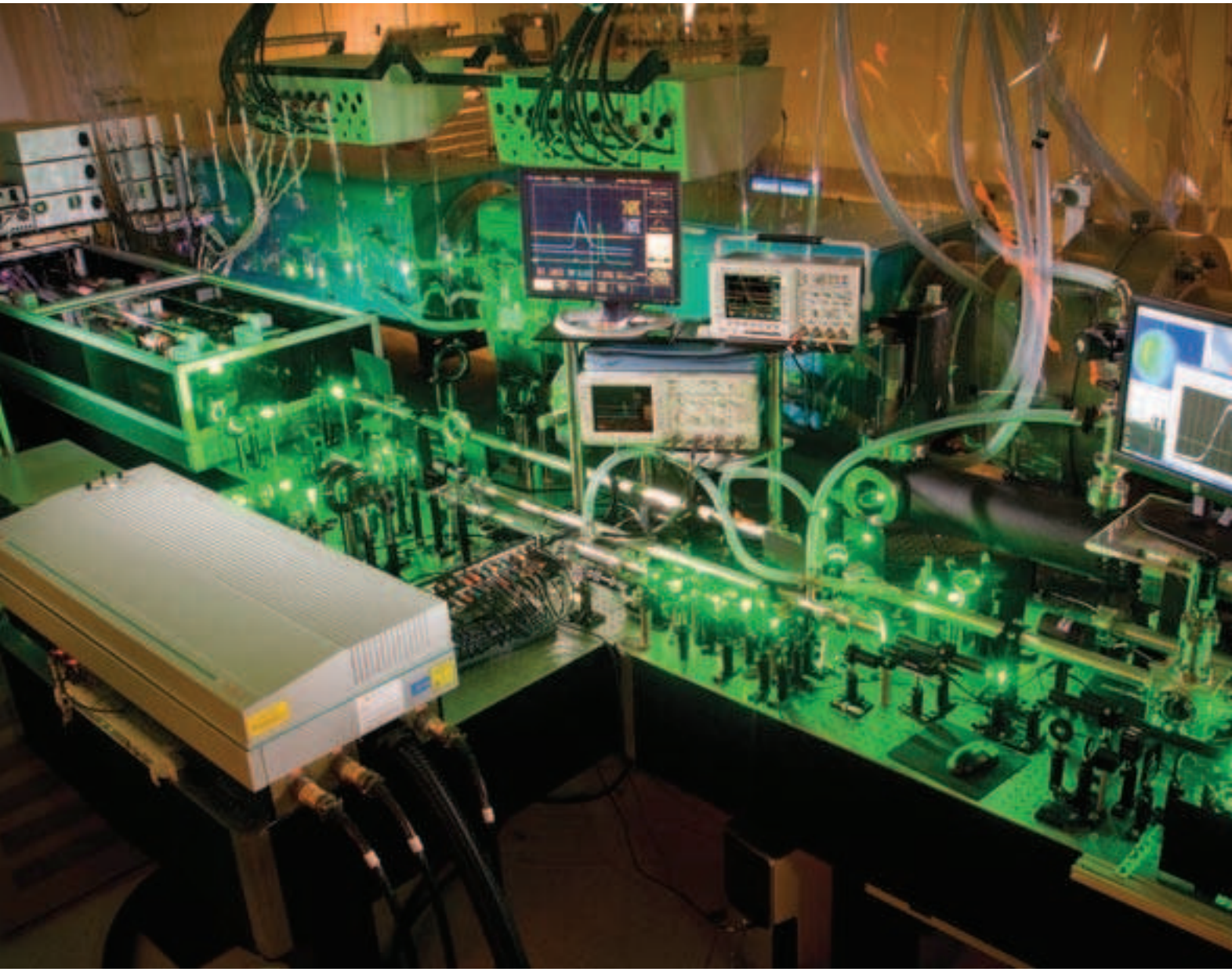
In 1954, Charles H. Townes, James P. Gordon (both at right), and Herbert J. Zeiger built the precursor to the laser—the maser, which emits microwaves instead of visible light. Their device used excited ammonia molecules to amplify the energy. Hydrogen masers (above) are still used for atomic clocks, because the microwave pulses emitted by hydrogen gas are extremely regular.

Soon after Maiman's demonstration, scientists proposed inducing nuclear fusion by concentrating laser beams on a tiny capsule of fuel to set off an atomic chain reaction, mimicking the conditions inside the sun. The resulting energy could be used in weapons or as a power source. The University of Rochester's Laboratory for Laser Energetics was one of the first facilities to explore using lasers, such as this one from 1972 (far right), for fusion energy.

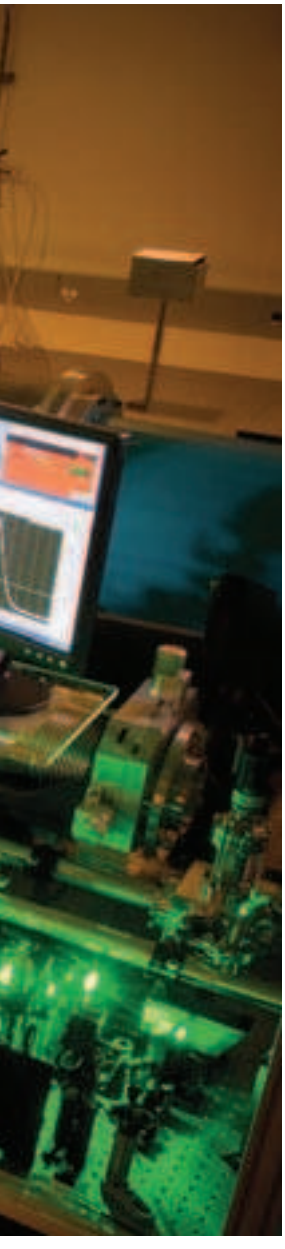


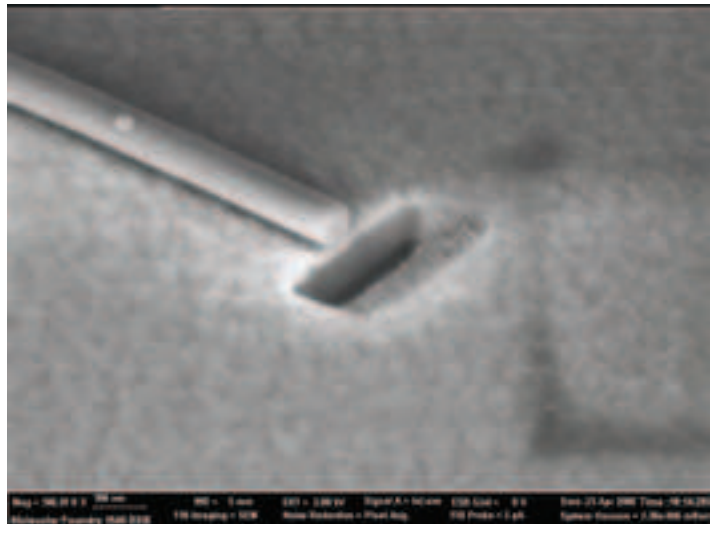
The Nova laser at Lawrence Livermore National Laboratory in California (left), completed in 1984, was the world's largest working laser until its retirement in 1999. With 10 laser beams, it was used for experiments on x-rays, astronomical phenomena, and fusion energy. In 1996, it was made into a petawatt laser, in which a short, intense pulse produced the highest power yet achieved: about 1.3 petawatts, or 1.3 quadrillion watts. Nova's parts have been used in other lasers, such as the petawatt laser at the University of Texas at Austin; said to be the most powerful working laser, it produces about 1.1 petawatts. Below, at UT Austin, an infrared beam and a green amplifying beam zigzag back and forth across a table. The infrared beam then travels through amplifiers (blue) recycled from Nova.

LAWRENCE LIVERMORE NATIONAL LABORATORY; EVAN WINSLOW SMITH/NATIONAL ENERGETICS (TEXAS)



LIGO LABORATORY, XIANG ZHANG LAB/UC BERKELEY





The Laser Interferometer Gravitational-Wave Observatory comprises two observatories, in Louisiana (above) and Washington, that are seeking the first direct evidence of gravitational waves—distortions in the curve of space-time. At each, a laser beam is split into two beams that travel back and forth along 2.5-mile mirrored arms many times before recombining. A gravitational wave would distort the space inside the arms by less than a thousandth the diameter of an atomic nucleus, forcing the beams slightly out of sync.

Researchers at the University of California, Berkeley, have created the smallest semiconducting laser (left), which could eventually be used for optical computing. A cadmium sulfide wire 50 nanometers in diameter generates visible light and holds it in a five-nanometer space.

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BIOPark

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- **Foster business partnerships**
- **Advance the commercialization of products**

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convention.bio.org

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Research the TR50 further with our database of companies: **technology review.com/tr50**

TR50 2010: THE WORLD'S MOST INNOVATIVE COMPANIES

To select the 50 most innovative companies in the world, the editors of *Technology Review* looked for those that over the last year have demonstrated their superiority at inventing technology and using it both to grow as businesses and to transform how we live. We identified the companies that have the most promising technologies, whether they are giant corporations or fledgling startups with initial venture capital investments. Then we examined their business models, their strategies for deploying and scaling up their technologies, and the likelihood that they will succeed. The result is the first annual TR50.

IAN ALLEN

A123 Systems
Using novel nanomaterials for batteries

a123systems.com
Founded: **2001**
Management: **David Vieau (CEO), Bart Riley (CTO)**
Employees: **1,689**
Revenues: **$90.2 million**
R&D: **$37.0 million**
Market cap: **$1.8 billion**

TECHNOLOGY Engineers at A123 have developed ways to manufacture new types of lithium-ion batteries that are safer than conventional versions and use less expensive elements. The materials are structured at the nanoscale in a way that enables them to charge and discharge quickly. **MARKET** The batteries are being sold for use in rechargeable power tools, which require large bursts of power and are often operated in harsh environments. But the far bigger long-term market is in electric vehicles and large-scale electricity storage: because they're safe and made from abundant elements, the batteries lend themselves to use in conventional hybrids, plug-in hybrids, and all-electric cars and are a good choice for storing power to help stabilize the electrical grid. **STRATEGY** A123 began by offering power-tool makers a product with capabilities that conventional battery makers couldn't match. Its first deal in that industry allowed it to scale up to making millions of batteries, which helped lead to contracts for hybrid buses and won the attention of automakers.

TR *"AN ELECTRIFYING STARTUP," MAY/JUNE 2008*

Adobe
Rich content for mobile

www.adobe.com
Founded: **1982**
Management: **Shantanu Narayen (CEO), Kevin Lynch (CTO)**
Employees: **7,335**
Revenues: **$3.0 billion**
R&D: **$565.1 million**
Market cap: **$17.8 billion**

TECHNOLOGY The company's Flash platform, which enables Web browsers to display media content such as video and animation, has become a standard. Its most recent version of the software is meant to bring that same capability to smart phones and netbooks, which used to lack the necessary processing power. Adobe is streamlining Flash to run under the constrained conditions in smaller devices, but it also benefits from the trend toward better processors in smart phones. **MARKET** About 17 percent of mobile-phone subscribers in the United States now have smart phones, and figures suggest that about 20 percent of mobile-phone users access the Internet from a phone. Adobe hopes to establish Flash as strongly in this growing market as it has done on desktops. **STRATEGY** Adobe sells developers software for creating Flash applications. In order to maintain its appeal to that market, it gives away software for running those applications to users all over the world. With its push into mobile platforms, the company hopes to attract the new class of developers writing applications for smart phones.

Akamai
Optimizing the Internet

www.akamai.com
Founded: **1998**
Management: **Paul Sagan (CEO), Michael Afergan (CTO)**
Employees: **1,500**
Revenues: **$834.0 million**
R&D: **$39.2 million**
Market cap: **$4.4 billion**

TECHNOLOGY For nearly a decade, Akamai's algorithms have played a critical role in finding the best routes for delivering content over the Internet, and they can determine where to host content in order to make its delivery as efficiently as possible. Recently, the company has introduced products such as a Web application firewall, which works "in the cloud" to stop attacks on rich Internet applications before the threatening traffic arrives at a customer's servers. **MARKET** Akamai says it delivers between 10 and 20 percent of all Internet traffic. Its customers include media companies, social networks, software makers, and the U.S. military. It stands to benefit from the increasing amount of rich, interactive content traveling over the Internet: the more complex a site is, the more it needs the company's services. **STRATEGY** Though the company is best known for content delivery, Akamai is expanding to appeal to businesses that want to deliver Web applications. The company bills its platform as a way for companies to avoid problems and vulnerabilities as more and more Web applications move into the cloud.

Alnylam
Targeting RNA to treat diseases

www.alnylam.com
Founded: **2002**
Management: **John Maraganore (CEO), Akshay Vaishnaw (senior VP, clinical research)**
Employees: **170**
Revenues: **$98.3 million**
R&D: **$96.9 million**
Market cap: **$712.5 million**

TECHNOLOGY Alnylam is creating a new class of drugs that target RNA. In theory, this approach can alter levels of any protein linked to a specific disease, either by directly silencing the RNA that codes for the protein or by targeting short RNA strands, called microRNAs, that regulate gene expression. **MARKET** The company is developing a wide range of drugs, focusing initially on treatments for Huntington's disease, liver cancer, high cholesterol, and a respiratory disease called respiratory syncytial virus. An offshoot company, Regulus, will focus exclusively on blocking microRNAs, initially in treatment of hepatitis C, cancer, cardiovascular disease, fibrosis, immune disorders, and metabolic diseases. **STRATEGY** Alnylam plans to develop and commercialize new drugs both alone and in coöperation with pharmaceutical partners. It has exclusive rights to fundamental patents on RNA interference and has formed alliances with Medtronic, Novartis, Biogen Idec, Roche, and GlaxoSmithKline; these deals have generated approximately $640 million in funding to date.

Amazon.com
Leading the new wave of e-readers

www.amazon.com
Founded: **1994**
Management: **Jeffrey P. Bezos (CEO), Werner Vogels (CTO)**
Employees: **20,700**
Revenues: **$21.7 billion**
R&D: **$1.0 billion**
Market cap: **$51.7 billion**

TECHNOLOGY Amazon.com led the charge in bringing electronic books into the mainstream with its Kindle e-readers. Thanks to its use of Sprint's 3G network, customers can download books seconds after placing an order, without having to plug the device into a computer. The technology also keeps track of readers' progress through books, even if they're reading on multiple Kindles, phones, or computers. **MARKET** Though Amazon hasn't released exact sales figures, the company says that Kindle is currently the best-selling product line on its site. The e-reader market heated up a great deal in the past year; in a 2009 report, Forrester Research predicted that the devices will go mainstream in the next couple of years, with more than five million U.S. consumers owning e-readers by 2011. **STRATEGY** Amazon.com has helped set consumer expectations regarding prices and distribution methods for e-books. Though Amazon faces intense competition in this market, especially now that Apple has introduced the iPad, the company has gained a head start by integrating the devices aggressively with its powerful retail site.

American Superconductor

Superconducting cables carry more electricity

www.amsc.com
Founded: **1987**
Management: **Gregory Yurek (CEO), Dan McGahn (COO)**
Employees: **519**
Revenues: **$250.2 million**
R&D: **$19.7 million**
Market cap: **$1.7 billion**

TECHNOLOGY A single cable made by American Superconductor can carry as much electricity as 10 equivalent sets of copper cables. The superconducting cables are woven from wires made of a material that shows no resistance to the flow of electricity when cooled to about –196 °C. Liquid nitrogen flows through the cables to achieve the correct temperature. **MARKET** With conventional cables, significant amounts of current are lost to resistance. They are almost always installed above ground, and miles of such wiring are typically needed to bring power from remote wind and solar farms to cities. Superconducting transmission lines can affordably be buried underground, and they could cut power losses substantially. The company says the annual market for underground electricity transmission is $9 billion. **STRATEGY** A proposed five-gigawatt substation in New Mexico would be a test for the new cables: the superconducting lines would connect the nation's three regional electrical grids so that they could share energy. If the project is approved, the system could be completed by 2014.

Apple

Building "the best" computers

www.apple.com
Founded: **1976**
Management: **Steven P. Jobs (CEO), Timothy D. Cook (COO)**
Employees: **34,300**
Revenues: **$36.5 billion**
R&D: **$1.3 billion**
Market cap: **$185.5 billion**

TECHNOLOGY From the "click wheel" navigation on its first iPods to the touch-sensitive screens on today's devices, Apple has pushed user interfaces forward dramatically; in 2009, it introduced the world's first multitouch mouse. Because of such successes, sales of its iPad tablet computer are eagerly anticipated. **MARKET** The company increased its share of the high-end (over $1,000) computer market from 66 to 91 percent between January 2008 and May 2009, according to the NPD Group, a market research firm. Although the iPhone had only 2.5 percent of the worldwide handset market, profit margins on the phone are so high that Apple made an estimated $1.6 billion from the device in the third quarter of 2009—more than any other cell-phone maker. **STRATEGY** The company focuses on design and user experience, tightly integrating its hardware, software, and services; the iTunes software and online music store, for example, form a complete ecosystem, as do the iPhone operating system and online app store. The company uses its strong cash position—$40 billion, with no debt—to develop innovative products in new areas.

Applied Materials

Saving solar costs with large-scale manufacturing

www.appliedmaterials.com
Founded: **1967**
Management: **Michael R. Splinter (CEO), Mark R. Pinto (CTO)**
Employees: **12,619**
Revenues: **$5.0 billion**
R&D: **$934.1 million**
Market cap: **$17.0 billion**

TECHNOLOGY Applied Materials makes equipment for manufacturing solar panels of unprecedented size, potentially reducing the price of solar power. The company, already an established leader in display technology, began its solar venture in 2006 and took just six months to develop equipment for manufacturing thin-film silicon cells. It now sells equipment for making the cells on pieces of glass with an area of 5.7 square meters. Working at this scale brings down the cost per watt of energy that the panels produce. **MARKETS** The company has a growing list of customers, mostly in Asia and Europe. In the fall, it opened a research and development center in Xi'an, China, to capitalize on a growing market it sees in that country. **STRATEGY** The new R&D center will focus on the needs of China's mostly urban population by developing technologies such as windows that harvest solar energy. The company will also continue research at its California site, hoping to raise the efficiency of solar panels produced with its equipment from 8.5 percent to 10 percent by year's end and to 12 percent by 2012.

TR *"SCALING UP SOLAR POWER," P. 84*

AthenaHealth

Electronic health records in the cloud

www.athenahealth.com
Founded: **1997**
Management: **Jonathan Bush (CEO), David E. Robinson (COO)**
Employees: **992**
Revenues: **$178.9 million**
R&D: **$10.6 million**
Market cap: **$1.4 billion**

TECHNOLOGY AthenaHealth has developed a Web-based system for electronic health records that takes advantage of cloud computing. Because the software is housed on servers rather than on a user's hard drive, the program is easy to update in order to adapt to new government mandates and other changes. The Web-based program also makes it easier for different health-care providers to share medical information. **MARKET** The market for clinical information systems is estimated at $8 billion to $10 billion annually. Hospitals and medical practices are increasingly moving toward adoption of electronic health records, thanks in part to financial incentives introduced by Congress in 2009. Medical practices that don't have electronic systems in place will face penalties beginning in 2015. These incentives have also increased competition among those selling the technology for electronic medical records. **STRATEGY** AthenaHealth has targeted small, physician-operated practices. The company also provides billing software and a system for managing doctor-patient communication.

DuPont

New types of biofuel similar to gasoline

www.dupont.com
Founded: **1802**
Management: **Ellen J. Kullman (CEO), Uma Chowdhry (CTO)**
Employees: **60,000**
Revenues: **$26.8 billion**
R&D: **$1.4 billion**
Market cap: **$29.6 billion**

TECHNOLOGY DuPont has partnered with BP to produce the transportation fuel butanol from agricultural feedstocks. Because biobutanol has a higher energy density than the leading biofuel, ethanol, consumers using it can drive more miles per gallon. **MARKET** Butanol will compete with ethanol as a transportation biofuel. But compared with ethanol, it's more similar to gasoline, which means it can be blended with conventional transportation fuels in higher proportions. The potential demand for biobutanol could thus be far greater than the demand for ethanol, and the fuel won't require changes in car technology. In addition, butanol can be transported through existing pipelines, so it doesn't necessitate the new infrastructure that would be required to distribute ethanol. **STRATEGY** DuPont and BP say that a demo plant to make butanol through the newly formed company Butamax should open this year. The company will also license the technology to other producers and is developing methods for making butanol from cellulosic sources like switchgrass instead of crops like corn and sugarcane.

First Solar

Pioneering innovative thin-film solar panels

www.firstsolar.com
Founded: **1999**
Management: **Rob Gillette (CEO), Bruce Sohn (president)**
Employees: **3,524**
Revenues: **$1.9 billion**
R&D: **$33.5 million**
Market cap: **$9.5 billion**

TECHNOLOGY A leading producer of thin-film solar panels, First Solar is pursuing an alternative to conventional silicon-based technology. The key is a material called cadmium telluride, which absorbs light better than silicon does; as a result, extremely thin films of the material are all that's needed. The panels are less efficient than silicon solar cells, but they're also cheaper. Low-cost manufacturing techniques have allowed the company to overtake manufacturers of silicon panels, significantly increasing its share of the market last year. **MARKET** Because the thin-film panels generate less power than silicon panels of similar size, the technology isn't particularly well suited for use on rooftops, where space is limited. It's best suited for large-scale utility projects in which panels are mounted on the ground. **STRATEGY** First Solar's priority has been to drive down manufacturing costs; in 2008 it broke the $1-per-watt barrier, which had seemed beyond reach for makers of conventional panels. It has also improved the efficiency of its modules to make them more competitive as it aggressively expands its business.

GE

Building the smart grid

www.ge.com
Founded: **1892**
Management: **Jeff Immelt (CEO), Mark Little (director, GE Global Research)**
Employees: **323,000**
Revenues: **$161.6 billion**
R&D: **$3.0 billion**
Market cap: **$172.0 billion**

TECHNOLOGY Pilot programs designed to make the electrical grid more efficient and reliable are using several GE products, including high-efficiency transformers, programmable thermostats, smart appliances, and meters that communicate real-time information on power consumption to utilities and customers. The company has set up a smart-grid lab to simulate the effects of introducing power from intermittent sources such as wind and solar and to study how two-way communication within the grid can make these renewable sources easier to integrate. **MARKET** Increased interest in reducing energy consumption has led to greater investment in communication and monitoring equipment intended to improve the electrical grid. Last year's Recovery Act, for example, included $4.5 billion for such smart-grid projects. **STRATEGY** Because GE has businesses that span all the parts of the grid, it is able to integrate those parts to make sure they work together. GE has won big contracts for smart-grid projects in cities including Miami and Tokyo.

TR *"LIFELINE FOR RENEWABLE POWER," JANUARY/FEBRUARY 2009*

GlaxoSmithKline

Tackling the diseases of aging

www.gsk.com
Founded: **2000**
Management: **Andrew Witty (CEO), Moncef Slaoui (chairman, R&D)**
Employees: **101,300**
Revenues: **$44.2 billion**
R&D: **$6.8 billion**
Market cap: **$102.5 billion**

TECHNOLOGY In 2008, GlaxoSmithKline acquired Sirtris, a startup based in Cambridge, MA, that is developing compounds to mimic the health benefits of resveratrol, a chemical that appears to combat an array of age-related ailments in rodents. In doing so, GSK became a leader in the search for drugs to treat diseases associated with aging. Sirtris's founders believe that its compounds change cells at the molecular level in the same ways achieved with caloric restriction—adherence to a nutritionally complete but very low-calorie diet shown to extend life span in mice, dogs, worms, and flies. **MARKET** Cancer, Alzheimer's disease, and diabetes are just some of the ailments directly related to aging. And as the populations of wealthy countries continue to age, the demand for therapies to treat such illness will continue to boom. Drugs for type 2 diabetes alone represent a $26 billion market. **STRATEGY** The company is broadly focused on a variety of diseases related to aging. It recently launched a clinical study in Europe of one of its resveratrol-mimicking compounds, SRT2104, in people with type 2 diabetes.

Google

Redesigning the operating system

www.google.com
Founded: **1998**
Management: **Eric Schmidt (CEO), Sergey Brin (CTO)**
Employees: **19,835**
Revenues: **$22.7 billion**
R&D: **$2.8 billion**
Market cap: **$172.4 billion**

TECHNOLOGY Perhaps Google's most important offering in the past year was the Chrome OS, an operating system designed to run Web applications. Because users store very little data locally, Chrome can employ a radical new security architecture that reinstalls the operating system if a check with Google's central servers determines that anything has become corrupted. **MARKET** Netbook vendors and chip manufacturers have agreed to build devices designed to run with Chrome. Whereas the traditional operating-system model aims to support more and more applications on a desktop computer, Google hopes that its brand will appeal to consumers looking for cheap computers designed for working on the Internet. **STRATEGY** The company's mantra "What's good for the Internet is good for Google" seems to figure heavily into its strategy for Chrome. Google hopes to enable and encourage users to rely even more heavily on the Internet, which will contribute to its bottom line through its search and productivity applications.

TR *"AN OPERATING SYSTEM FOR THE CLOUD,"* SEPTEMBER/OCTOBER 2009

HTC

Hunting for the iPhone killer

www.htc.com
Founded: **1997**
Management: **Cher Wang (CEO), Horace Luke (chief innovation officer)**
Employees: **7,168**
Revenues: **$4.8 billion**
R&D: **$293.2 million**
Market cap: **$8.1 billion**

TECHNOLOGY In 2008, HTC became the first company to develop cell phones for use with Google's Android mobile operating system. Last June, the Taiwan-based manufacturer announced a user interface for its smart phones that sits on top of the Android OS; among other things, it allows users to set up different profiles for work and home. The company most recently collaborated with Google on the design of the Nexus One phone, which the search company is selling directly to consumers. **MARKET** HTC is the fourth-biggest maker of smart phones, with 6.5 percent of the market worldwide. While overall sales for mobile phones remained flat in the third quarter of 2009, smartphone sales grew almost 13 percent from the same quarter in 2008, according to the market research firm Gartner. **STRATEGY** By partnering directly with Google as well as with mobile carriers, HTC has leaped ahead of many other cell-phone makers in the Android market. Early technology adopters and business analysts alike are betting that an Android device is the most likely candidate to emerge as an "iPhone killer."

IBM

Packaging cloud services for clients

www.ibm.com
Founded: **1896**
Management: **Samuel J. Palmisano (CEO), John E. Kelly III (director, IBM Research)**
Employees: **398,455**
Revenues: **$95.8 billion**
R&D: **$5.8 billion**
Market cap: **$164.6 billion**

TECHNOLOGY In 2009, the company launched a set of cloud-computing services offering, among other things, virtual desktops and an environment for testing applications. Instead of supplying generic storage and processing power that can be used for whatever a customer needs, IBM's cloud platform is designed to work for specific types of tasks, such as analytics, that it thinks would be most useful to companies. **MARKET** IBM's entry into cloud computing plays to its historic strengths in working with larger corporations. It allows those companies to buy cloud services without sacrificing the benefits of working with a traditional company. **STRATEGY** IBM hopes to appeal to customers who have hesitated to take advantage of cloud computing by simplifying the process and giving them a clear sense of how cloud services can be used. It also hopes to assuage companies' worries about the security of cloud computing. Customers can set up cloud-style architecture on their own servers to increase their efficiency without entrusting all their data to a third party.

TR *"SECURITY IN THE ETHER," JANUARY/FEBRUARY 2010*

Illumina

The fastest-growing genomics company

www.illumina.com
Founded: **1998**
Management: **Jay T. Flatley (CEO), Mostafa Ronaghi (CTO)**
Employees: **1,536**
Revenues: **$646.7 million**
R&D: **$100.0 million**
Market cap: **$4.6 billion**

TECHNOLOGY Illumina sells two major types of genomics technology. In the first, microarrays dotted with specific snippets of genetic information detect common genetic variations; scientists have used them to conduct large genomic studies on everything from human diseases to milk production in cows. Recently, the company also began marketing a sequencing machine capable of reading entire genomes. The device can read a human genome for $10,000. **MARKET** Illumina microarrays and sequencing machines are used by research centers, pharmaceutical companies, academic institutions, and biotechnology companies. Although the market is now mainly in research, it is expected to broaden as the price of sequencing falls. A growing number of pharmaceutical and agricultural companies are incorporating genomic information into product development. **STRATEGY** Illumina dominates the sequencing market. It is also the only large company in the personal-genomics arena, offering a $48,000 sequencing service that can be ordered online with a physician's prescription.

Infinera

Tiny components for ultrafast optical networks

www.infinera.com
Founded: **2000**
Management: **Tom Fallon (CEO), Drew Perkins (CTO)**
Employees: **937**
Revenues: **$318.3 million**
R&D: **$80.4 million**
Market cap: **$707.1 million**

TECHNOLOGY Infinera builds photonic integrated circuits—systems that incorporate all the components necessary for optical data transmission into a single pair of chips. Transmitting data on light beams requires lasers that send the light, multiplexers that split it up or recombine it, modulators that encode it with data, and detectors that receive it. In March the company announced that it had packed all these elements onto chips that deliver 400 gigabits of data per second—enough to carry 1.2 million YouTube videos—and use half the power of its original chips. **MARKET** Infinera sells its equipment to companies that build optical networks, including communications companies, cable companies that are beginning to extend fiber-optic networks to homes, and Internet content providers. **STRATEGY** It is taking advantage of increasing bandwidth demand on undersea networks by adapting its equipment to work with them. Its simplified network design allows for rapid deployment, and because the technology is more energy efficient than the equipment typically used in these networks, operating costs are lower.

Intel

Pushing silicon further

www.intel.com
Founded: **1968**
Management: **Paul S. Otellini (CEO), Justin R. Rattner (CTO)**
Employees: **79,800**
Revenues: **$35.1 billion**
R&D: **$5.7 billion**
Market cap: **$111.8 billion**

TECHNOLOGY In 2009, the world's largest maker of semiconductor chips announced research on several new technologies: thermoelectric systems to cool microchips, a single-chip cloud-computing system, and an optical cable that will be able to transfer 10 gigabits of data per second between gadgets. **MARKET** Intel builds chips used in machines from high-powered servers to desktop computers to consumer electronics. In the second quarter of 2009, it accounted for 80.6 percent of global microprocessor revenue, according to market research firm iSuppli—its highest market share since 2005. The total microprocessor market is estimated at over $35 billion for the year. **STRATEGY** One way the company has continued its rapid development cycle is by increasing its academic partnerships for long-term research, situating labs near institutions such as the University of California, Berkeley; the University of Washington; and Universitat Politècnica de Catalunya, in Barcelona, Spain. These labs are investigating optical computing, tiny "mote-sized" sensors, and transistors made from carbon nanotubes.

iRobot

Bringing robots to the masses

www.irobot.com
Founded: **1990**
Management: **Colin Angle (CEO)**
Employees: **514**
Revenues: **$287.6 million**
R&D: **$17.6 million**
Market cap: **$423.5 million**

TECHNOLOGY The company makes robots that can move in complex environments, such as a messy living room or a battlefield, by means of a proprietary system that coördinates navigation, mobility, manipulation, and sensing so that the machine can respond efficiently to changing circumstances. Last year, iRobot showed off a prototype for small, intelligent, disposable military robots. **MARKET** Its automated vacuum cleaner, the Roomba, is arguably the first robot to find success in the consumer marketplace; more than five million have sold since it was introduced in 2002. The Roomba was followed by a host of other home cleaning robots designed for single functions, such as one that cleans pools and another that cleans gutters. The company also manufactures robots for the U.S. Army. **STRATEGY** By developing relatively affordable consumer robots for limited purposes, iRobot has edged out competitors offering more expensive products. The home robots are affordable because they are not extremely precise; instead, they focus on performing one task well and relatively quickly.

Medtronic
Stimulating the brain

www.medtronic.com
Founded: **1949**
Management: **William A. Hawkins (CEO), Stephen N. Oesterle (senior VP, medicine and technology)**
Employees: **37,665**
Revenues: **$15.1 billion**
R&D: **$1.4 billion**
Market cap: **$48.2 billion**

TECHNOLOGY More than a decade ago, Medtronic introduced deep brain stimulation, a technique in which surgically implanted electrodes deliver a series of electrical pulses to a specific part of the brain. Since then, the company has continued to improve this technology and broaden its applications. In 2009, the U.S. Food and Drug Administration approved it for use in treating obsessive-compulsive disorder. **MARKET** Deep brain stimulation is currently approved to treat Parkinson's disease, dystonia, and obsessive-compulsive disorder. More than 60,000 people around the world have received Medtronic's therapy to date. The company is now testing the technology as a treatment for medication-resistant depression and epilepsy. **STRATEGY** Medtronic has emerged as a leader in commercializing neurotechnology, or devices that actively intervene in the brain's processes. It is also well positioned to exploit the new field of optogenetics, which allows researchers to control brain cells with light rather than with pulses of electricity. Perhaps one day physicians will be able to use the technique therapeutically.

Nanosphere
Diagnostic tests for personalized medicine

www.nanosphere-inc.com
Founded: **2000**
Management: **William Moffitt (CEO); Greg Shipp (chief medical officer)**
Employees: **166**
Revenues: **$1.7 million**
R&D: **$23.7 million**
Market cap: **$158.2 million**

TECHNOLOGY Nanosphere makes clinical diagnostic tests that are two to three times as sensitive as those commonly used in hospital labs today and much simpler, taking just hours rather than days or weeks to complete. The company's instruments, which use microfluidics to pull DNA and proteins from a sample, detect genetic variations in blood that make some drugs more effective in some patients than others. The key is an array of gold nanoparticles studded with chemicals that capture characteristic proteins and nucleic acids from clinical samples such as blood. **MARKET** The company's Verigene instrument was approved late last year by the U.S. Food and Drug Administration for use in pharmacogenomic testing. **STRATEGY** The company first targeted the market for predicting how a patient will react to the anticoagulant warfarin. It is also developing a test for use with Plavix, an anticlotting drug that fails to benefit patients with a particular genetic variant. Nanosphere also plans to move into the market for oncological and other tests, as well as environmental sensing of bioterror and infectious-disease agents.

Nissan
Bringing electric vehicles to the masses

www.nissanusa.com
Founded: **1933**
Management: **Carlos Ghosn (CEO); Mitsuhiko Yamashita (executive VP, R&D)**
Employees: **186,336**
Revenues: **$93.4B**
R&D: **NA**
Market cap: **$36.6 billion**

TECHNOLOGY This year, Nissan is rolling out an all-electric car that will use advanced lithium-ion batteries and should be able to run about 100 miles on a charge. The dashboard will display detailed information about the state of the batteries and the location of charging stations. In contrast to the bulky batteries used in earlier electric vehicles, the battery pack is a flat device that sits under the seats, leaving ample room inside the vehicle. **MARKET** The car's range is more than long enough to cover the daily travel of 80 percent of drivers in major markets, such as the United States. But experts say that most Americans prefer cars they can use for long road trips, so the vehicle could be used mostly as a second, commuter car. **STRATEGY** Nissan plans to sell the car at about the same price as a comparable conventional vehicle and then lease the battery. The company says that the cost of the lease plus the cost of charging the battery will be less than the cost of gasoline for a typical driver. Nissan plans to help pay for the batteries by finding secondary uses for them once they've exceeded their useful life in the car.

Prime View International
Supplies low-energy displays for every major e-reader

www.pvi.com.tw
Founded: **1992**
Management: **Scott Liu (CEO)**
Employees: **3,178**
Revenues: **$380.2 million**
R&D: **NA**
Market cap: **$1.7 billion**

TECHNOLOGY Last year, Prime View International acquired the electronic-paper company E Ink, whose technology, originally developed at MIT's Media Lab, uses a small pulse of electricity to move charged particles in a flexible film in order to change the image on the screen. The resulting display is easier than liquid-crystal displays to read in direct sunlight and saves energy by drawing electricity only when the picture needs to be changed. And because it's made on a flexible plastic film, it's lightweight and durable. **MARKET** With its acquisition of E Ink, Prime View International now controls the entire market for e-reader displays. More than five million e-readers were sold in 2009, and 12 million will be sold this year, according to research firm iSuppli. All major models use E Ink's technology, including Amazon's Kindle, Plastic Logic's Que, and Sony's e-reader. **STRATEGY** So far the company has been selling black-and-white displays, but other companies are developing electronic paper capable of displaying color and video. Prime View International is now looking to develop those capabilities itself.

Suntech
Making solar power more affordable

www.suntech-power.com
Founded: **2001**
Management: **Zhengrong Shi (CEO), Stuart Wenham (CTO)**
Employees: **9,070**
Revenues: **$1.5 billion**
R&D: **$15.3 million**
Market cap: **$2.4 billion**

TECHNOLOGY Suntech is the world's largest producer of crystalline-silicon solar panels, the most common type. It specializes in multicrystalline cells, which produce somewhat less power per square meter than single-crystal cells but yield a competitive price per watt because the materials cost less. The company has broken an efficiency record for multicrystalline cells that had stood for 15 years; one key to the accomplishment was to increase the amount of light the cells absorb by texturing their surface and decreasing the thickness of electron-conducting wires. **MARKET** Suntech's cells are efficient enough to be practical for commercial and residential rooftops, where space is limited. But they're also inexpensive enough to be selected for large, utility-scale installations. **STRATEGY** Based in Wuxi, China, Suntech has announced plans to build a 30-megawatt-capacity factory in Phoenix, AZ. It also has a strong sales presence in Germany. The company is continuing to increase the efficiency of its solar panels, and has designed modules that are cheaper to install for utility-scale projects.

Amyris

Developing next-generation biofuels

www.amyrisbiotech.com
Founders: **Jay Keasling, Jack D. Newman, Kinkead Reiling, Neil Renninger (2003)**
Management: **John Melo (CEO), Neil Renninger (CTO)**
Funding: **$170 million**
Key investors: **Khosla Ventures, Kleiner Perkins Caufield and Byers**

TECHNOLOGY Amyris has engineered yeasts and other microörganisms to convert sugars into hydrocarbons that can be hydrogenated to make diesel fuel. The result burns cleaner than fossil-based diesel, reducing emissions of sulfur, nitrogen oxides, and particulates. **MARKET** Unlike ethanol, today's leading biofuel, hydrocarbons can be distributed through the same pipelines as conventional fuels. They can also be pumped with existing fuel pumps and used in conventional vehicles, so they have a larger potential market than ethanol. **STRATEGY** The company is making biofuels from sugarcane because making them from corn is too expensive. Last year, Amyris opened a demonstration plant in Brazil, which has extensive infrastructure for biofuel production. Later this year, the company will begin converting part of a sugarcane mill into its first production facility, and eventually it will contract with independent mills. Amyris would also like to make fuels from low-cost cellulosic materials such as switchgrass, but the technology for breaking them down into sugar is still too costly.

TR *"SEARCHING FOR BIOFUELS' SWEET SPOT," P. 46*

Bind Biosciences

Improving drug delivery

www.bindbio.com
Founders: **Robert Langer, Omid Farokhzad (2007)**
Management: **Scott Minick (CEO), Jim Wright (CSO)**
Funding: **$29.5 million**
Key investors: **Polaris Venture Partners, Flagship Ventures, Arch Venture Partners, DHK Investment**

TECHNOLOGY Bind has developed nanoparticles that deliver cancer drugs more precisely to malignant cells and help the drugs circulate longer in the body. Biodegradable polymers surrounding a drug allow it to diffuse slowly into the bloodstream, while a coating of polyethylene glycol—a molecule with waterlike properties—helps the particles evade detection by the immune system. Their surface is sprinkled with peptides designed to bind to the tumor cells to make sure the payload reaches its target. **MARKET** The technology could theoretically be applied to any existing drugs or experimental compounds that would benefit from longer circulation times or better targeting. It might also revive experimental drugs that have been shelved because of problematic side effects; the improved delivery system could make them effective at lower doses. **STRATEGY** Bind plans to develop its own therapeutics and to partner with pharmaceutical and biotechnology companies to develop their molecules for drug approval. The startup is initially focusing on chemotherapy drugs, which can trigger intolerable side effects at high doses.

Complete Genomics

Sequencing human genomes to order

www.completegenomics.com
Founders: **Clifford Reid, Radoje Drmanac, John Curson (2006)**
Management: **Clifford Reid (CEO), Radoje Drmanac (CSO)**
Funding: **$91 million**
Key Investors: **OVP Venture Partners, Genentech**

TECHNOLOGY Complete Genomics makes machines that can sequence human genomes quickly and cheaply, thanks in part to a new way of packing DNA onto specially fabricated arrays with unprecedented density. The company aims to reduce costs by increasing volume; it hopes to be able to sequence a genome for $5,000 by later this year or 2011. **MARKET** Complete Genomics sells its services only to institutions, not to individuals. Eight human genomes cost approximately $20,000 apiece as a batch; sequencing giant Illumina, by contrast, will sequence an individual's genome for $48,000. **STRATEGY** The company offers its sequencing service to such organizations as academic labs and pharmaceutical companies. Focusing solely on human genomes allows it to operate this service more efficiently. And because everything is done in-house, the company hasn't had to spend time or money making its machines consumer-friendly. It is building the world's largest sequencing facility and a massive data center to manage the huge volumes of information it will produce.

Coskata

Making ethanol from garbage

www.coskata.com
Founders: **Todd Kimmel, Rathin Datta (2006)**
Management: **William Roe (CEO), Richard Tobey (VP, R&D)**
Funding: **$69.5 million**
Key investors: **GM, Khosla Ventures, GreatPoint Ventures**

TECHNOLOGY Biofuels are typically made in one of two ways: by fermenting sugars with the help of microbes or in chemical reactions usually carried out under high temperatures and pressures. Coskata combines the two processes. Materials such as wood chips and old tires are processed in high-temperature, high-pressure conditions to produce hydrogen and carbon monoxide, and then microörganisms turn those gases into ethanol. **MARKET** Incentives such as government mandates to use renewable fuels are helping to create a market for advanced biofuels. But a technology for making biofuels isn't much use unless it works with local source materials, and most processes are specialized to work only with specific feedstocks. Coskata's process can easily make fuel from a wide range of materials, opening up markets in more places. **STRATEGY** Coskata will license its technology to other companies, such as established biofuel producers. It has developed a modular system with elements that companies can mix and match according to their needs.

eSolar

Generating large-scale, low-cost electricity

www.esolar.com
Founder: **Asif Ansari (2007)**
Management: **John Van Scoter (CEO); Craig Tyner (senior VP, engineering)**
Funding: **$170 million**
Key investors: **Idealab, Oak Investment Partners, Google.org**

TECHNOLOGY The company uses arrays of tens of thousands of mirrors to focus sunlight on a central tower, producing intense heat that turns water into steam to generate electricity. The mirrors are installed on prefabricated metal frames that allow them to pivot and tilt to track the sun throughout the day and from season to season. Proprietary software ensures that all the mirrors are aimed properly. **MARKET** The technology is ideal for the utility-scale solar power that could meet needs like those of California, where utilities are required to produce 20 percent of their electricity from renewable sources this year. U.S. projects that eSolar has in the works will produce up to 500 megawatts of power, and the company has announced projects in China and India that will produce 3,000 megawatts in all. **STRATEGY** The system is an improved version of solar thermal technology; previous versions used enormous mirrors, often over 40 feet wide, that were difficult to manufacture and install. The company says it has cut costs by using smaller mirrors, which are still effective because they are numerous and automatically controlled.

Fate Therapeutics

Screening drugs with stem cells

www.fatetherapeutics.com
Founders: **Philip Beachy, Sheng Ding, Randall Moon, David Scadden, Leonard Zon (2007)**
Management: **Paul Grayson (CEO), Dan Shoemaker (CTO)**
Funding: **$50 million**
Key investors: **Genzyme Ventures, Polaris Venture Partners**

TECHNOLOGY The company licenses novel technology for creating induced pluripotent stem (iPS) cells—adult cells that have been chemically reprogrammed to resemble embryonic stem cells, which can differentiate into different types of adult tissue. Fate's reprogramming technique relies on proteins and other small molecules rather than genetic engineering, making the resulting cells more appropriate for therapeutic use. **MARKET** Drug companies are interested in this technology for drug development and toxicity testing. Scientists can use iPS cells to create different types of tissue, such as heart or brain cells, and then test an experimental compound on the tissue to determine whether it harms the cells or whether it enhances or blocks a particular molecular process. In addition, the iPS cells might one day be used to generate replacements for damaged tissue. **STRATEGY** Fate plans to use the cells for its own drug development program. It will also partner with companies and researchers who want to use the technology for toxicity testing, drug discovery, disease modeling, or cell therapy.

Fluidigm

Flexible microfluidics

www.fluidigm.com
Founders: **Stephen Quake, Gajus Worthington (1999)**
Management: **Gajus Worthington (CEO), Robert C. Jones (VP, R&D)**
Funding: **$190 million**
Key investors: **Alloy Ventures, Lehman Brothers Venture Capital Group, Lilly BioVentures, GE Equity**

TECHNOLOGY Fluidigm has developed microfluidic chips that can precisely control nanoliters of liquid. Scientists can use these chips to analyze gene expression in single cells, to identify mutations in cells, and to grow stem cells under controlled biological conditions. **MARKET** Microfluidics is now used mainly in biomedical research labs; Fluidigm sells its chips to them for use in processes such as gene sequencing, single-cell analysis, and agricultural genotyping. The technology could give rise to cheap, disposable diagnostic devices for a variety of applications. Ultimately, Fluidigm hopes to be a significant player in clinical applications such as prenatal diagnostics and cancer diagnostics. **STRATEGY** The chips are made from a flexible polymer that can be easily and cheaply adapted to many functions. Because the technology makes it possible to perform new types of analysis, such as controlling the growth environment of single cells, the company hopes it will find entirely new applications and broaden the market for microfluidics.

TR *"SHOVELING WATER," JANUARY/FEBRUARY 2010*

Hulu

Bringing premium TV content to the Web

www.hulu.com
Founders: **News Corp., NBC Universal (2007)**
Management: **Jason Kilar (CEO), Eric Feng (CTO)**
Funding: **$100 million**
Key investors: **Providence Equity Partners, Walt Disney Company, News Corp., NBC Universal**

TECHNOLOGY Hulu's technology allows consumers to stream television shows and movies free over the Internet; the content includes several brief commercial spots, and the company has been exploring ways to target these ads. The user interface was developed in-house, but Adobe provides the core technology for the embedded video player, and Akamai manages the content delivery network. **MARKET** Consumers are drawn to Hulu by its premium content. Advertisers favor it, especially over other video sites, both because of that content and because most videos on Hulu have just a few ads, giving each more impact. The company could face competition from cable companies, which are likely to become more aggressive in courting the Web audience, and from Netflix, which can stream content on demand. **STRATEGY** The audience for TV shows is moving away from television sets and toward the Web, and Hulu has positioned itself at the center of the transition. In the long term, it apparently seeks to be a leader in the market for premium Web content.

Joule Biotechnologies

Making biofuels from sunlight

www.joulebio.com
Founders: **Noubar Afeyan, David Berry (2007)**
Management: **William Sims (CEO), Dan Robertson (senior VP, biological sciences)**
Funding: **Not disclosed**
Key investor: **Flagship Ventures**

TECHNOLOGY Joule has engineered microbes that harness the sun's energy to convert carbon dioxide and water directly into ethanol or hydrocarbon fuels. When housed in bioreactors in sunny areas, the company says, the organisms produce 20,000 gallons of biofuel per acre per year. The process offers an advantage over making biofuels from corn or cellulose, because growing those materials requires large amounts of land. It's also an improvement over using photosynthetic algae to make biofuel precursors, as some other companies do, because those chemicals must then be processed to make fuel. **MARKET** The company says its products will be competitive with petroleum-based fuels if crude oil is priced at $50 per barrel or more. **STRATEGY** Joule is currently building its first pilot plant, in Leander, TX, and says it will be operational in the first half of this year. The company, which plans to use the plant to demonstrate the scalability of its technology, expects to produce ethanol commercially by the end of this year; it plans to demonstrate large-scale production of hydrocarbon fuel in 2011.

Luxtera

Transmitting data faster

www.luxtera.com
Founders: **Alex Dickinson, Cary Gunn, Axel Scherer, Eli Yablonovitch (2001)**
Management: **Greg Young (CEO), Cary Gunn (CTO)**
Funding: **$72.8 million**
Key investors: **New Enterprise Associates, Sevin Rosen Funds, August Capital, Freescale Semiconductor**

TECHNOLOGY Luxtera designs silicon photonics, optical circuits that are fully integrated with electronics and made using standard microchip manufacturing techniques—so the devices are less expensive and also orders of magnitude smaller (and thus in many cases faster) than traditional photonic elements. The company launched its first product, an optical active cable, in 2007. In November, it announced an optical transceiver that makes it possible to send data between chips at 10 gigabits per second, using very little power. **MARKET** The company's optical interconnects are designed for use in supercomputing clusters, telecommunications equipment, and large data centers. Its optical cables can be used over longer distances than previous high-performance interconnects, while its new chips will make optical data transmission possible within high-performance computing systems. **STRATEGY** Luxtera is focused on high-performance systems that need to send and receive data very quickly. Ultimately, it hopes photonic networking will replace the copper wires still used to send data over relatively short distances.

Novomer

Sustainable plastics made from carbon dioxide

www.novomer.com
Founders: **Geoffrey Coates, Tony Eisenhut, Scott Allen (2004)**
Management: **Jim Mahoney (CEO), Ron Valente (VP, R&D)**
Funding: **$21 million**
Key investors: **OVP Venture Partners, Physic Ventures, Flagship Ventures, DSM Venturing**

TECHNOLOGY A cobalt-based catalyst developed by founding chemists from Cornell University facilitates the reaction of petroleum compounds with carbon dioxide or carbon monoxide to form common plastics used in packaging, electronics cases, and absorbent materials. The process sequesters the greenhouse gases and can be used to make biodegradable plastics. **MARKET** The company hopes to compete with producers of conventional industrial polymers made entirely from petroleum. Novomer emphasizes the green aspect of its products to capitalize on consumer concerns about the environment, but the primary advantage of making polymers from carbon gases is that it's cheaper, which may help the company grab market share. **STRATEGY** Earlier this year, Novomer partnered with Dutch chemical giant DSM to develop compounds called polyols for use in coatings for food packaging and in automobile and industrial finishes. Other polyols on the market are made with bisphenol A, a suspected carcinogen. The Novomer/DSM product, which will be marketed as BPA-free, will be made of 50 percent carbon dioxide.

Obopay

Bringing payment services to phones

www.obopay.com
Founder: **Carol Realini (2005)**
Management: **Carol Realini (CEO), John Tumminaro (CTO)**
Funding: **$126 million**
Key investors: **Nokia, Qualcomm, Redpoint Ventures**

TECHNOLOGY With Obopay, mobile-phone users can transfer money to each other over the Web, or they can use an application installed on the device to do so by means of a text message. The company's technology keeps the transaction secure and notifies the sender and receiver of its status. **MARKET** In the United States, Obopay targets people who want a substitute for cash transactions; for example, friends can use the service to split up a restaurant bill. Elsewhere, the company markets itself as a way to encourage customers to open bank accounts even when they don't have easy access to banking infrastructure. **STRATEGY** Obopay hopes to capitalize on the large population of mobile-phone users in places, such as India, where wired Internet access and conventional banking services are often limited. Mobile payment services have received attention recently, in part because cell phones are common even in remote and poorer areas. The company collects a fee for each transaction—from the user for U.S. transactions or from the bank for transactions in other countries.

Pacific Biosciences

Accurate sequencing in real time

www.pacificbiosciences.com
Founder: **Stephen Turner (2004)**
Management: **Hugh Martin (CEO), Stephen Turner (CTO)**
Funding: **$266 million**
Key investors: **Wellcome Trust, Mohr Davidow Ventures, Kleiner Perkins Caufield and Byers, Alloy Ventures**

TECHNOLOGY The company has a way to continuously record the sequence of individual DNA molecules; that approach might prove faster than other gene sequencing methods, reducing costs. Its machines are set to go on sale in the second half of 2010, and the company predicts that by 2013, it will be able to sequence a person's genome in 15 minutes for less than $1,000. **MARKET** Fast, cheap sequencing has broad applications—from sequencing cancer genomes and infectious diseases to use in clinical diagnostics and even crop breeding. The company plans to sell its devices to research institutes and pharmaceutical and agricultural companies. **STRATEGY** Other companies are developing their own advanced sequencing techniques, but what sets Pacific Biosciences' technology apart is that it can read longer strands of DNA molecules. That makes it easier to assemble the pieces into a complete genome, and it may also prove important for some medical applications. The ability to analyze single copies of a molecule may have applications beyond sequencing as well.

TR *"INTERPRETING THE GENOME," JANUARY/FEBRUARY 2009*

Plastic Logic

A novel e-reader

www.plasticlogic.com
Founders: **Stuart Evans, Richard Friend, Henning Sirringhaus (2000)**
Management: **Richard Archuleta (CEO), Martin Jackson (VP, technology)**
Funding: **$200 million**
Key investors: **Dow Venture Capital, BASF Venture Capital, Siemens Venture Capital**

TECHNOLOGY Plastic Logic has announced a new e-reader, the Que, that is the first to use transistors based on organic polymers rather than silicon. Organic transistors make it possible to use a plastic backing instead of glass, resulting in a reader that's thin, flexible, lightweight, and extremely durable. **MARKETS** In the market for e-readers—which is expected to boom over the next several years—Plastic Logic differentiates itself by targeting businesspeople. The letter-page size of the Que makes it a good choice for reading documents, magazines, and newspapers, and the device has a search feature that's useful for transferring and sorting through documents, including Excel files, PowerPoint presentations, and PDFs. It can also display e-mail and calendars from Microsoft Exchange. The company plans to release a BlackBerry app. **STRATEGY** Not only is its device technologically novel, but Plastic Logic's focus on the business executive rather than the book-loving consumer could help create a niche for the company in the fast-growing e-reader market.

Serious Materials

Making greener building materials

www.seriousmaterials.com
Founders: **Kevin Surace, Marc Porat (2002)**
Management: **Kevin Surace (CEO), Brandon Tinianov (CTO)**
Funding: **$120 million**
Key investors: **Enertech Capital, New Enterprise Associates, Navitas Capital, Saints Capital**

TECHNOLOGY The company's drywall takes 80 percent less energy to make than ordinary drywall and uses manufacturing processes that emit less carbon dioxide. One version does double duty as an insulator, reducing heating and cooling costs for buildings. Serious Materials also makes lightweight windows incorporating a thin film that acts as an insulator. **MARKET** The company says the annual U.S. market for its materials is over $22 billion for windows, over $6 billion for drywall, and over $15 billion for insulation. Twelve percent of buildings that went up in 2008 were certified by the U.S. Green Building Council; the proportion is projected to grow to 25 percent by 2012, and the company's products can help builders win that certification. **STRATEGY** Betting that many building owners will find retrofitting existing structures more cost-effective than building new ones, Serious Materials is developing products to insulate windows instead of replacing them. Next year, it will treat the 6,500 windows in the Empire State Building, a project that's expected to save almost 40 percent on the building's energy costs.

Solyndra

Novel solar-panel design captures more energy

www.solyndra.com
Founder: **Chris Gronet (2005)**
Management: **Chris Gronet (CEO), Ben Bierman (executive VP, operations and engineering)**
Funding: **$970 million**
Key investors: **CMEA Capital, Virgin Green Fund, Rockport Capital, Argonaut**

TECHNOLOGY Solyndra's solar panels are cylindrical, so they capture more sunlight than traditional flat panels and can produce more electricity. And they can be packed more tightly by being arranged horizontally into modules that resemble pencils in a box. The rolled-up shape is possible because the panels are made of a nonconventional semiconductor (copper indium gallium selenide), not rigid silicon. The shape saves on installation costs because less hardware is required to hold the cells in place; whereas a strong gust will lift up an unprotected flat panel, it flows around the horizontally arrayed Solyndra cells. **MARKET** Solyndra targets the commercial rooftop market. By the company's estimate, there are 11 billion square meters of such surface that could be filled with solar cells. **STRATEGY** Not only do the cells produce more electricity per rooftop, but because they require less in the way of supportive hardware, buildings that can't support heavy modules could be fitted with Solyndra's systems. In December, the company filed with the Securities Exchange Commission in preparation for going public.

StreamBase

Dealing with high volumes of real-time data

www.streambase.com
Founders: **John Partridge, Michael Stonebraker, Richard Tibbetts (2003)**
Management: **Mark Palmer (CEO), Richard Tibbetts (CTO)**
Funding: **$37 million**
Key investors: **Accel, Bessemer Venture Partners, Highland Capital Partners, In-Q-Tel**

TECHNOLOGY Companies are pushing to incorporate data from the real-time Web into news feeds and search results. Though Twitter posts are a key part of that effort, not all real-time data is directly created by people; huge quantities are collected automatically as users visit websites, watch streaming video, and interact with online advertisements. All this data is relevant right away for companies that want to adjust their sites to user behavior, but it's traditionally been collected into batches and processed after the fact. StreamBase has created databases structured in such a way that information can be processed as it's collected. **MARKET** Streambase markets itself to organizations that handle large volumes of real-time data. It started in the financial sector, which accounts for 80 percent of its customers; it also sells its product to government agencies seeking to process intelligence. **STRATEGY** The increasing amount of data available over the Internet has inspired the company to court new classes of customers, including e-commerce sites, companies offering location-based services, and online gaming sites.

Synthetic Genomics

Making fuel from algae

www.syntheticgenomics.com
Founders: **J. Craig Venter, Hamilton O. Smith, Juan Enriquez, David Kiernan (2005)**
Management: **J. Craig Venter (CEO), Hamilton O. Smith (CSO)**
Funding: **Not disclosed**
Key investors: **Draper Fisher Jurvetson, BP, ExxonMobil**

TECHNOLOGY Strains of algae engineered by Synthetic Genomics excrete oils that could be refined to make biofuels, including varieties such as gasoline and diesel. The company efficiently studies many strains of algae, using high-throughput methods to help identify those that produce large amounts of the desired oils and to reveal techniques for engineering known strains in ways that will increase their oil production. **MARKET** Ethanol is the leading biofuel today, but the market for it is constrained by the difficulty of distributing it and using it in vehicles. Demand could be much greater for biofuels that can be produced at existing refineries, distributed in existing pipelines, and used in most vehicles. **STRATEGY** The company has formed a partnership with ExxonMobil, which has agreed to invest up to $300 million in Synthetic Genomics. The project is intended to find and develop strains of algae using Synthetic Genomics' expertise and to draw on ExxonMobil's knowledge in order to develop large-scale production methods.

Tesla Motors

Putting high-performance electric cars on the road

www.teslamotors.com
Founders: **Martin Eberhard, Elon Musk, Marc Tarpenning (2003)**
Management: **Elon Musk (CEO), JB Straubel (CTO)**
Funding: **$269.5 million**
Key investors: **Daimler AG, Draper Fisher Jurvetson, Sergey Brin, Larry Page**

TECHNOLOGY Tesla has developed a battery pack, electric motor, and digital controllers that keep its electric cars running smoothly. Its sports car can accelerate as fast as the best gas-powered cars, reaching 60 miles per hour in 3.6 seconds. The company is now developing a less expensive electric sedan. **MARKET** By 2015, the market for electric vehicles in the United States is expected to reach 50,000 annually. So far, Tesla's vehicles have dominated the market for high-performance electric cars. The first car the company has produced for sale costs over $100,000 and is not widely available (1,000 have been shipped). But its new sedan, expected in 2012, will cost about $50,000 after federal tax credits. **STRATEGY** Tesla set out to change the image of electric cars with a high-performance vehicle styled like a traditional sports car. It decided to use lithium-ion battery cells that are already mass-produced for consumer electronics, even though they are very expensive. As lithium-ion cells come down in price, the company will be able to make less expensive vehicles.

TR *"TESLA ROADSTER," SEPTEMBER/OCTOBER 2008*

1366 Technologies

Cutting the cost of solar power

www.1366tech.com
Founders: **Emanuel Sachs, Frank van Mierlo (2007)**
Management: **Frank van Mierlo (president), Emanuel Sachs (CTO)**
Funding: **$17.6 million**
Key investors: **Polaris Venture Partners, North Bridge Venture Partners**

TECHNOLOGY The manufacturing method that 1366 developed for silicon solar cells increases the amount of light the cell can absorb by reducing the area that's shaded by electron-conducting wires and by decreasing the amount of light reflected off the surface. Increasing the light absorption helps increase the power output of the cell, effectively decreasing the cost per watt. The company is also developing a way to make solar wafers—the thin sheets of silicon that serve as the core of a solar cell—in a process that's simpler than current techniques and wastes less silicon. **MARKET** Because they are efficient, the company's cells are particularly well suited for rooftops, where space is at a premium. They can also be used for ground-based utility-scale power plants. **STRATEGY** Rather than make its own solar cells in the short term, 1366 plans to sell equipment to existing manufacturers around the world. Processes that are compatible with current manufacturing equipment, the company says, should allow its technology to be adopted quickly. Its long-term plans are to start manufacturing solar cells on its own.

Tilera

Multiplying multicore chips

www.tilera.com
Founders: **Anant Agarwal, Vijay Aggarwal, Devesh Garg (2004)**
Management: **Omid Tahernia (CEO), Anant Agarwal (CTO)**
Funding: **$50 million**
Key investors: **Bessemer Venture Partners, Columbia Capital, Quanta Computers, Walden International**

TECHNOLOGY Tilera makes multicore computer chips that link large numbers of microprocessors in a type of mesh network. This network allows each core to share information with other processors on the chip more easily and quickly than is possible through an on-chip bus interconnect (a sort of central intersection through which data must flow to get between the cores of a traditional multicore chip). In October, the company announced that it had used its own 64-bit processors to build the world's first 100-core chip. **MARKET** Tilera's 64-core chip has been used in cellular towers, graphics processing, videoconferencing systems, Internet Protocol–based TV systems, and hardware that monitors Internet traffic to reduce spam and viruses. Its newest chip, intended for more general-purpose computing applications, is aimed at the high-profit server market. **STRATEGY** Tilera plans to expand beyond special-purpose embedded processors and to tackle Intel head-on by selling server chips. Its newest chip is designed for high-end networking and telecommunications; it should ship later this year.

Twitter

Setting the standard for real-time communication

www.twitter.com
Founders: **Jack Dorsey, Biz Stone, Evan Williams (2007)**
Management: **Evan Williams (CEO), Douglas Bowman (creative director)**
Funding: **$160 million**
Key investors: **Union Square Ventures, Spark Capital, Benchmark Capital**

TECHNOLOGY Twitter provides a social-networking service that revolves around 140-character messages called "tweets." Posts on Twitter can be sent and received with mobile phones, over the Web, or through a wide variety of third-party desktop programs. The company also built an interface that makes it easy for other websites to pick up feeds of data from the updates that users provide constantly. **MARKET** Though Twitter has struggled to find a business model, it's had no trouble attracting users. As of July 2009, according to Nielsen, it was the third-largest mobile social-networking site in the United States, with over four million users (behind Facebook and MySpace). **STRATEGY** Twitter has recently made deals with Google and Microsoft's Bing search engine, both of which spotlight tweets as part of their efforts to include more real-time search results. The deals put Twitter in a strong position to take advantage of the growing possibilities of the real-time Web. Speculation continues about whether the company will launch advertising within Twitter feeds.

TR *"CAN TWITTER MAKE MONEY?" P. 52*

Ushahidi

Open-source humanitarianism

www.ushahidi.com
Founders: **Erik Hersman, Ory Okolloh (2008)**
Management: **Ory Okolloh (executive director), Erik Hersman (director of operations)**
Funding: **$1.8 million**
Key investors: **Humanity United, Omidyar Network**

TECHNOLOGY Ushahidi is an open-source technology designed to make it easy for people in any part of the world to collect information about a crisis. Users can send reports by text message, e-mail, or Web postings, and the software aggregates them and organizes the data into a map or timeline. **MARKET** Ushahidi's software was first used in early 2008 to track violent outbreaks related to the disputed Kenyan election of 2007. Al Jazeera employed it to monitor activity in Gaza in early 2009, and it was used to spread information about shelters and damaged buildings after the earthquake that struck Haiti in January. The company thinks the software should be widely useful to help local populations stay informed in an emergency and communicate their needs and problems with experts and interested parties elsewhere. **STRATEGY** Ushahidi is managed as a nonprofit organization that distributes the tool and helps coördinate the community of volunteers supplying reports. Its founders have so far supported Ushahidi with funds donated by humanitarian organizations such as Humanity United.

Yelp

Speaking out about local businesses

www.yelp.com
Founders: **Jeremy Stoppelman, Russel Simmons (2004)**
Management: **Jeremy Stoppelman (CEO), Russel Simmons (CTO)**
Funding: **$56 million**
Key investors: **Elevation Partners, Benchmark Capital, DAG Ventures**

TECHNOLOGY Yelp collects reviews from customers of local businesses and makes it easy for others to find those reports online. The company says a key part of its technology is the automated filter that it uses to screen out potentially fraudulent reviews. Yelp has also created applications for the iPhone, Android, BlackBerry, and Palm Pre. The iPhone app recently gained a location service, allowing users to check in when they visit a business. **MARKET** Yelp aims its review site at people looking to patronize local businesses. It makes money from advertising sold to businesses hoping to reach this audience, though the company stresses that advertising and reviews function independently of each other. **STRATEGY** Yelp reportedly refused an acquisition effort by Google late last year. Since then, the company has focused on enhancing its offerings for mobile phones, adding location-based services and augmented-reality features. Yelp hopes to demonstrate that its users are more engaged than those of any other similar technology, thereby winning advertising dollars from local businesses.

Zynga

Selling virtual goods for social games

www.zynga.com
Founders: **Mark Pincus, Michael Luxton, Eric Schiermeyer (2007)**
Management: **Mark Pincus (CEO), Michael Luxton (CTO)**
Funding: **$219 million**
Key investors: **Kleiner Perkins Caufield and Byers, Union Square Ventures**

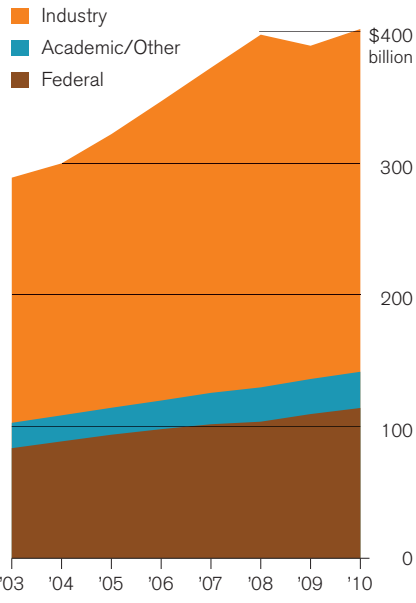
TECHNOLOGY The company designs casual games that can be played in brief spurts over a long period of time. Its games include a social element, giving users a new way to interact with friends online or on smart phones. As a result, the key technologies that Zynga exploits are the application programming interfaces available on most social networks today, such as Facebook Platform and Google's OpenSocial. The company offers casino games, simulations, and role-playing games. It has become well known for titles such as Farmville, Mafia Wars, and CafeWorld. **MARKET** Zynga is aimed squarely at users of social-networking sites such as Facebook. The company claims to have 200 million monthly active users across all games. **STRATEGY** The company makes money by charging users for virtual goods, such as virtual tractors that make it easier to till the land in Farmville. Though it makes some of its money from advertising, it says that 90 percent of its revenue comes from the virtual goods, which are reportedly purchased by a million users each month.

50

WHO SPENDS THE MONEY?

While government spending has increased in the last several years, industry remains by far the largest source of funding.

TOTAL R&D FUNDING (2003–2010)

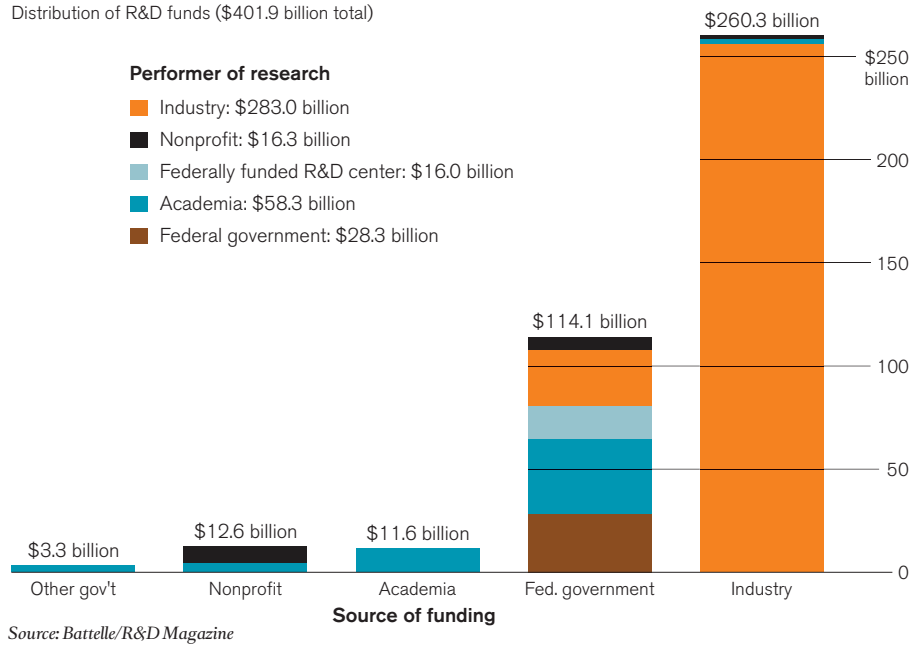


Sources: National Science Foundation's National Patterns of R&D Resources 2007 and Battelle/R&D Magazine

Industry funds most of its own research, but it also receives a significant amount of support from the federal government, as does academic research.

U.S. R&D SOURCES AND PERFORMERS (2010 estimates)

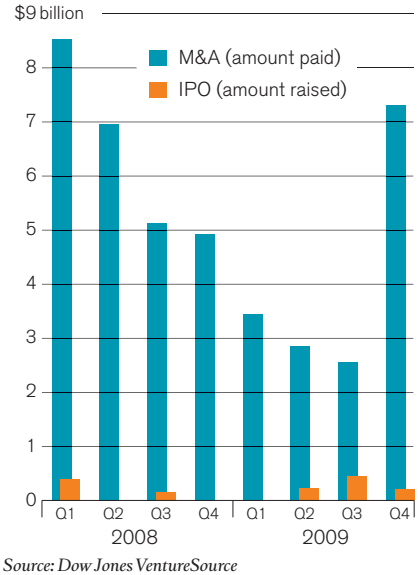
Distribution of R&D funds ($401.9 billion total)



Source: Battelle/R&D Magazine

The opportunities for venture-backed companies to gain a payday, either through a merger or acquisition or by going public, bounced back at the end of last year.

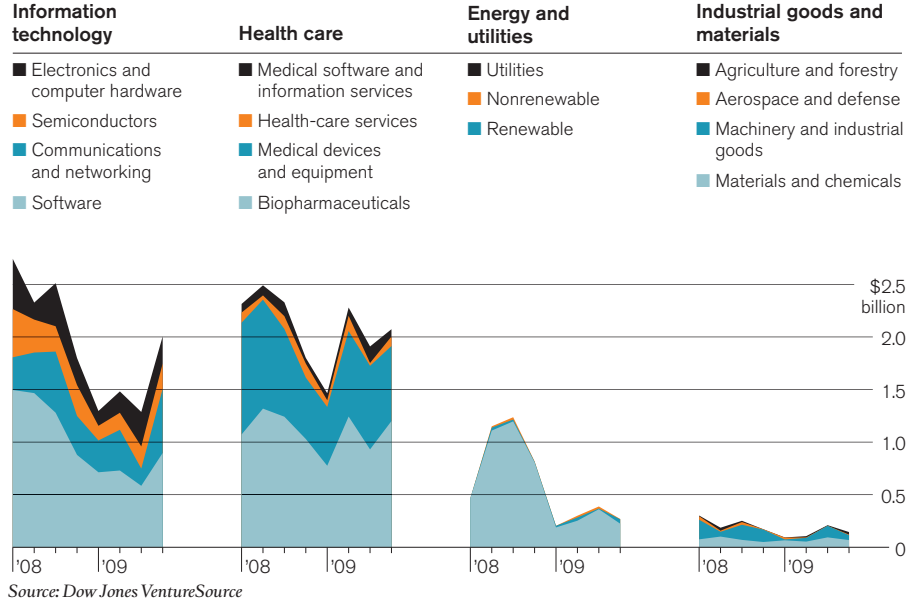
U.S. VENTURE-BACKED ACTIVITY (2008–2009)



Source: Dow Jones VentureSource

Software and biopharmaceuticals remain the favorite investments of venture capitalists, but both areas had a somewhat bumpy 2009, recovering slightly at the end of the year. Investment in renewable energy, despite the attention it often receives, is still relatively small.

TOTAL QUARTERLY INVESTMENT (2008–2009)



Source: Dow Jones VentureSource

TOMMY McCALL

SUGAR NATION Workers stockpile sugar at a sugarcane mill in the Brazilian state of São Paulo. Brazil is the world's largest producer and exporter of sugar. The country may play a key role in producing the next generation of biofuels.

Searching for Biofuels' Sweet Spot

California-based Amyris has used breakthroughs in synthetic biology to reinvent biofuels. To turn its technology into an industrial process, it has headed to the land of sugar: Brazil.

By ANTONIO REGALADO

The four-lane Anhangüera Highway leads northwest from Brazil's financial capital, São Paulo, into some of the most productive agricultural land in the world. The view from a car window reveals plantations of hairy eucalyptus trees and cow pastures rife with termite mounds. Fields of sugarcane roll out of sight over the hilltops.

Turn right at kilometer 104.5 and you enter Techno Park, a tidy corporate research neighborhood that looks as if it has been torn out of suburban California. And in a way, it has. In a building not far from the entrance are rows of neatly organized workstations, shiny fermentation tanks, and clanking centrifuges. All this machinery is a near-exact replica of the equipment at a facility in Emeryville, CA. Even the coat racks are the same.

The building is the Brazilian outpost of Amyris Biotechnologies, a U.S. research outfit celebrated for its work under a grant from the Bill and Melinda Gates Foundation to make a scarce malaria drug more widely available. Its founder, Jay Keasling, is considered a pioneer of synthetic biology, and the malaria project, which could save many thousands of lives, has been featured in the *New Yorker*. Last May, Keasling was awarded the Biotechnology Industry Organization's first Biotech Humanitarian Award.

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Less well publicized is that Amyris has raised more than $170 million in venture capital to get itself into the biofuels business and that its current plans call for producing nearly all that fuel in Brazil. Roel Collier, a Belgian fluent in Portuguese who heads Amyris's Brazil operations, points to a 12-meter-tall steel tank in which genetically

Photographs by NOAH FRIEDMAN-RUDOVSKY

modified yeast is feasting on the juice of the sugarcane that is so abundant in this country. "Inside is cutting-edge American technology applied to the competitive advantage of Brazil," he explains.

For the last two years, Collier's responsibilities have included shipping drums of frozen Brazilian sugarcane juice to Amyris's California laboratory, some 10,000 kilometers away. There, scientists have been genetically rewiring ordinary yeast cells to digest *caldo de cana,* as the juice is called, and turn it into farnesene, a fragrant oil that Amyris has shown can be converted into diesel fuel. In the fast-moving field of synthetic biology—a discipline that looks to rewrite the DNA of microörganisms as if it were computer code—the California laboratories of Amyris are considered state of the art. Researchers create and test tens of thousands of engineered yeast strains each week. The company employs nearly as many PhD yeast geneticists as all the universities in Brazil.

But Brazil offers Amyris one critical advantage over the United States: the economic conditions there lend themselves to exploiting the technology commercially. Brazil is the world's most efficient producer of sugar. Huge mounds of it pile up at the country's 420 sugarcane refineries. With its tropical weather and aggressive business culture, the country dominates the global sugar trade. And enormous supplies of inexpensive sugar are the key to making Amyris's technology practical.

"The reason to go to Brazil was pretty clear; it's the cheapest, most readily available source of sugar to power the technology platform," says Keasling, a professor of biochemical engineering at the University of California, Berkeley, who also heads the Joint BioEnergy Institute, a $135 million effort funded by the U.S. Department of Energy to extract sugars from wood chips, grass, and other inexpensive plant matter. In 10 to 15 years, its work could make sugar molecules as cheap to obtain in the U.S. as they currently are in Brazil. For now, though, the U.S. biofuels industry continues to make ethanol by fermenting the glucose in corn kernels. And corn is a relatively costly source of sugar, as the American ethanol industry has discovered to its distress. Despite taxpayer subsidies, U.S. manufacturers have not been able to turn consistent profits.

The story is different in Brazil, where sugarcane mills have been turning out inexpensive ethanol since the government launched a push for fuel independence in the 1970s. The country's automobile fleet now consumes more ethanol than gasoline. Nearly 90 percent of cars manufactured in Brazil can run on the biofuel. The industry has realized that "geography is destiny," says Mark Bunger, research director at Lux Research, a New York firm that studies the commercialization of emerging technologies. In Bunger's view, only a few places on the planet have the rain, sun, and land mass needed to make biofuels at the scale and price that can have a real impact. "The understanding that we are coming to is that it's never going to happen in some places," he says, "and Brazil is the first place where the economics make sense."

For many synthetic biologists, diesel is just the beginning. They believe that in principle, they can create microörganisms to produce replacements for any petroleum product. But there are huge risks.

Amyris reached a similar conclusion about three years ago—hence its identical fermentation labs in Emeryville and Brazil. Scientists in California tinker with yeast to make it convert sugar to farnesene more quickly; then the bugs are airmailed south for testing under tropical conditions. This year, Amyris plans to begin construction of a towering fermentation complex in the Brazilian state of Goiás. When it's done, it should be able to produce 100 million liters of green diesel fuel every year.

Like ethanol, Amyris's fuel will be made by fermenting sugar. But company scientists have redesigned yeast so that the microbes process it into combustible hydrocarbons instead of alcohol. That means the competition for its green fuel is not ethanol but diesel made from petroleum and also biodiesels made from vegetable oil or animal fat. Amyris says its fuel has a number of advantages over both. Unlike fossil fuels, it is made from a renewable source. It also contributes less greenhouse gas to the atmosphere: the company calculates that its Brazilian-made diesel will emit about 80 percent less greenhouse gas than conventional diesel. And compared with other biodiesels, its sugar-based fuel will be cheaper to make and will enable engines that use it to run better. Amyris's CEO, a former oil executive named John Melo, has been negotiating with companies that are looking for a green fuel, including Federal Express, Virgin Atlantic, and General Electric.

For many synthetic biologists, diesel is just the beginning. They believe that in principle, they can create microörganisms to produce replacements for any petroleum product. But there are huge risks. Amyris's yeast strains have proved unexpectedly vulnerable. And as with other biotechnology processes that depend on live microörganisms, no one can say if green diesel production can be scaled up economically from the 1,000-liter batches produced today. "All the forecasts are based on efficiencies of scale for processes that have never been run at those scales," says Noubar Afeyan, CEO of Flagship Ventures in Cambridge, MA, and a cofounder of LS9, a competing synthetic-biology startup. A major challenge is that it "takes hundreds of millions of dollars to prove it, even at medium scale."

Nine years ago, Amyris's technology was still a bench project in Keasling's Berkeley laboratory. Researchers had been looking at ways to coax microörganisms to produce commercially useful

FEEDSTOCK A sugarcane plantation near the city of Campinas. Each acre yields enough sugarcane juice to make 3,000 liters of ethanol.

products. By adding DNA from plants and bacteria, Keasling's lab eventually designed new bacteria and yeast cells that could make large quantities of isopentenyl pyrophosphate. With its five carbon atoms, the chemical is a sort of Lego block of the natural world; from it, plants and animals build isoprenoids, members of a large class of molecules that includes the anticancer drug taxol, vitamin E, and scents such as those of grapefruit and the pheromones of female cockroaches.

Keasling knew the invention was valuable, and in 2001 he filed the first patent application of his career. "We wanted to apply the tools to a real problem," he says. The chance came in 2004, when the Bill and Melinda Gates Foundation decided to donate $42.6 million to a project that would manufacture the antimalaria drug artemisinin with the aid of Keasling's made-to-order microbes.

Artemisinin is currently derived from the sweet wormwood plant, grown mostly in Africa and Asia. Supply of the drug is unsteady, and prices swing wildly; they reached $1,100 a kilogram in 2006. By using genetically modified yeast to produce it from sugar, Keasling's approach promised to solve the supply problem and dramatically cut the price. With its chance of saving thousands—perhaps millions—of people who might otherwise die of malaria, the project has become a symbol of synthetic biology's potential to change the world for the better. The Gates money paid for the rapid expansion of Amyris, which Keasling and three of his postdocs founded to carry out the malaria project. By late 2005, says Amyris's chief technical officer, Neil Renninger, some at the company were spending "nights and weekends" thinking about what other problems their technology could solve.

Amyris estimates that the isoprenoid family includes some 50,000 different types of molecules, so it was far from clear where to focus next. "When we began pitching the VCs, we said there are some drugs we think are interesting, and nutraceuticals, and even fuels—what do you think?" recalls Renninger. But it was hard to find a project as meaningful to Amyris's scientists as malaria. "This was really a culture of people that want to save lives and not make a lot of money," he says. "So when you throw making grapefruit flavor in front of them—well, it's not too interesting."

Things started changing by mid-2006, when two of Silicon Valley's best-known venture capital firms, Kleiner Perkins Caufield and Byers and green-energy specialist Khosla Ventures, offered to invest $20 million in the company. The U.S. Congress had passed renewable-fuel mandates in 2005, setting off a wave of speculative investment in all sorts of biofuels. Geoffrey Duyk, a managing director at TPG Biotech, which also put money into the company, recalls that once Amyris accepted the funds, the investors "came in and moved the focus to fuels."

The investors began courting Melo, then head of British Petroleum's North American fuels business, to be Amyris's CEO. Melo was running what he calls a "nice little business" involving huge truck fleets and scores of terminals, generating $34 billion in revenue. When a recruiter first called him about a biotech company with a malaria project, he recalls, "My reaction was, 'You have got to be kidding. I am a fuels guy, so what do I care?'"

As he learned more about synthetic biology and met Amyris's scientific staff, Melo changed his mind. Fuels are the largest of all businesses by revenue, but as a percentage of profits, oil companies spend only tiny sums on R&D and almost nothing on basic research. Melo decided his old industry was ripe for change. "The ability to modify microbes [means] we can be the Microsoft of fuels and chemicals, where we are in effect writing the software that goes into the fermentation tank," he says. "That, to me, was game changing." Melo directed the company to work on diesel, the world's most widely used transportation fuel and one that is often in short supply. Producing the right type of molecule proved surprisingly easy. Within six weeks, the scientists had switched a single enzyme in their artemisinin-producing bugs and begun producing farnesene, the oil they had identified as a potential precursor to diesel.

"They look like very different projects—one is a medicine and one is a fuel—but the metabolic route is similar," Collier says. "That was the big advance of Amyris." Farnesene is a pleasant-smelling oil that accounts in part for the odor of apple skins. By performing one additional chemical step, hydrogenation, Amyris can turn the yeast-produced farnesene into farnesane, a highly combustible fuel with properties similar to those of diesel.

As a hydrocarbon like diesel and gasoline, farnesane won't be subject to the problems that have affected other biofuels, Amyris is betting. Ethanol, for example, can mix with water, which may cause trouble when water makes its way into gasoline pipelines. Plant-derived biodiesels, meanwhile, contain impurities and can clog engines at low temperatures. Farnesane, on the other hand, can be simply dropped into the existing fuel distribution network. It even has an advantage over ordinary diesel: it contains no polluting sulfur.

But the project will have an impact only if it can be deployed at a massive scale. And no one is yet sure how well synthetic biology will work at such scales. Synthetic Genomics, a company started by

gene-sequencing pioneer J. Craig Venter, reached a $300 million agreement with ExxonMobil last year to develop fuel-producing algae. Yet Exxon's vice president for research and development, Emil Jacobs, told the *New York Times* that he didn't want to "sugar-coat" the project's chances. "For transportation fuels, if you can't see whether you can scale a technology up, then you have to question whether you need to be involved at all," he said.

The ability to make fuels in astonishing quantities isn't the only thing needed for them to become a realistic option. They are also commodities that are sold at rock-bottom prices. The petroleum industry's product, liter for liter, is half the price of Coca-Cola. Where were the main costs going to be in Amyris's production process? If ethanol-industry averages held true, the sugar its yeast feed on would represent over half the final price of making farnesane.

Those calculations were part of what led Melo to "plant the flag firmly in Brazil," recalls investor Duyk. American corn, though close at hand, would have been a poor bet. By 2007, booming U.S. ethanol production had sent corn prices soaring so high that tens of thousands of Mexicans demonstrated over the cost of tortillas. When oil prices fell in 2008 and corn prices remained at record levels, many U.S. ethanol makers could no longer make a profit.

Scale, cost, and competition with food supplies aren't the only issues for biofuels. Amyris wanted to market its diesel as good for the environment; its brochures claim that its "No Compromise" fuels will release 80 percent less carbon dioxide into the atmosphere than fossil fuels. Today, Brazilian sugarcane is the only crop that can possibly back up Amyris's green marketing. Brazilian studies say that sugarcane ethanol yields about 7 to 10 times as much energy as it takes to produce the fuel; in contrast, ethanol made from corn yields just slightly more than producing it consumes. While the environmental impact of growing sugarcane remains in dispute, it's clear that the process requires less energy than cultivating corn. What's more, Brazil's biofuel producers are more efficient than those in other countries, partly because many Brazilian mills burn sugarcane waste to power their crushers and distillers, reducing the use of fossil fuels.

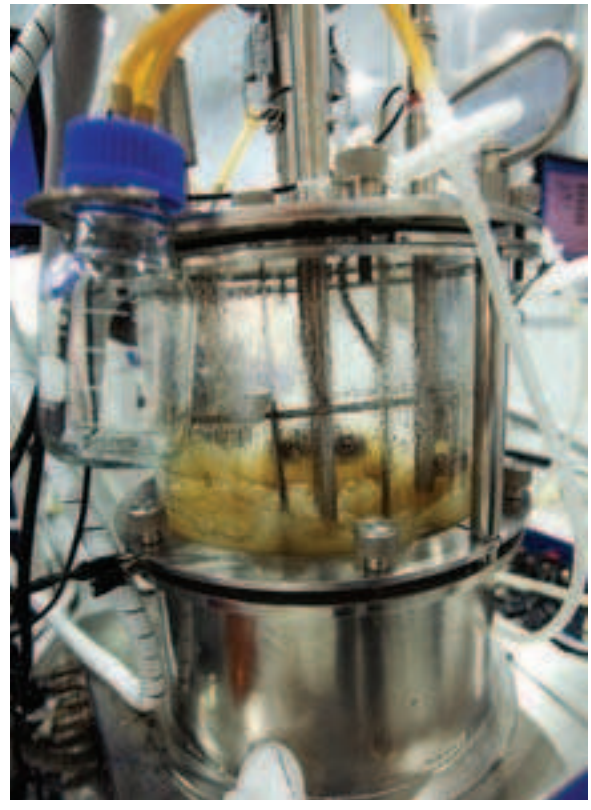
As a market, Brazil may bring other advantages, too. The country's demand for diesel is high, so Amyris could build a respectable business without ever exporting a drop. Brazil also has space to increase production: sugarcane is now planted on about 3 percent of Brazil's arable land, but the crop could expand onto more than 100 million acres currently used for grazing cattle. "You could probably quadruple and quintuple the cane production," says Bill Haywood, the CEO of LS9 and a former oil company executive. "That is poorly understood by the rest of the world. I think that Brazil is going to be the birth of high-quality green diesel, just as it was for ethanol."

In December, Amyris reached an agreement to build its first farnesene plant, a 100-million-liter-per-year facility that will be

constructed inside the newly built Boa Vista sugar and ethanol mill in Goiás. As part of the transaction, Amyris agreed to buy a 40 percent stake in the mill from its owner, Grupo São Martinho. Its total payment, around $80 million in cash and stock, was the highest price ever paid for milling capacity in Brazil, according to São Martinho's president, Fábio Venturelli. Amyris wanted control over the construction of its first big plant, to make sure it goes smoothly. But eventually the company plans to barter its technology for access to sugarcane juice, a less expensive approach. The idea is to have Brazil's sugar mills pay to retrofit their plants while Amyris contributes its genetically modified yeast. Amyris would then sell the farnesene and divide the profits with the mill.

Although the commercial terms may be complicated, the basic pitch Amyris is making isn't: in an industry that in many ways is low tech (more than half of Brazil's sugarcane is still hacked down by machete-wielding day laborers), it promises to turn mills into futuristic biorefineries capable of turning out chemicals and fuels more

www Take a tour of Amyris's plant outside Campinas, Brazil: **www.technologyreview.com/amyris**



YEAST FACTORY At Amyris's demonstration facility in Brazil, hydrocarbons are produced in a fermentation tower (far left). Inside a fermenter (above left), genetically modified yeast metabolizes sugar and produces farnesene, a fragrant hydrocarbon oil. Above, yeast strains are tested for efficiency. At left, a worker holds bottles of Amyris's final product, diesel fuel.

valuable than sugar or ethanol. Many Brazilian companies have been thinking along similar lines. When Venturelli became São Martinho's CEO in 2008 and first saw the blueprints for the Boa Vista mill, he noticed that someone had written a note on a blank area. It read, "This space for future sugarcane-based chemical."

Plenty of questions remain, though. "All our companies are searching to be at the forefront of the fuels market, and they see in Amyris the chance for technology transfer," says Alfred Szwarc, a technical advisor to UNICA, Brazil's largest sugarcane association. "But since we don't know the price or the operational costs, for now it's a lot of speculation."

The major uncertainty is how Amyris's yeast will perform under industrial conditions. It will be one of the first times synthetic biology has reached such a scale, and the process is certain to pose engineering problems no other company has faced before. One concern: wild yeast strains could ride into the fermentation tanks along with the sugarcane juice. In sterile lab experiments, that's not a problem. But in a sugarcane mill, yeast that doesn't make farnesene could easily overwhelm the lab-created variety.

Recent developments in the artemisinin project also suggest that costs could be an issue. Drug maker Sanofi Aventis, which agreed to handle commercial production of the antimalarial, says it ran into unexpected obstacles and now plans to produce the drug for $350 to $400 per kilo. That is close to the average price of the plant-derived version, but it's three to four times as expensive as Keasling has promised in media interviews.

In Brazil, Amyris's dreams of transforming the global fuel business may need to be deferred, at least for a time. The company's first facility may not produce farnesene cheaply enough to compete head to head with diesel. Instead, the farnesene produced by the São Martinho mill will initially be sold to the consumer-products market, where it may command prices far higher than what's paid for diesel. (It can be used, among other things, as a moisturizing agent for lipsticks or antiaging creams.)

That means Amyris's scientists may have to wait a while longer to change the world. But Melo says the company has not backed away from its goal of becoming a major force in the fuels market. "We are all about impact," he says. "Saving thousands of children is impact. With fuels, it's scale. If we can't scale our contribution to CO_2 [emissions] or green production, we will be irrelevant." TR

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Can Twitter Make Money?

Twitter plans to become the leader in instant news—and make itself into a sustainable business in the process.

By DAVID TALBOT

At the microblogging company Twitter's San Francisco headquarters, in the sixth-floor conference room, founder Evan Williams was declining to tell me anything about the company's strategies to earn revenues when, suddenly, his cofounder Biz Stone blurted, "Whoa!" It was 10:10 A.M. on January 7, and it would prove to be the latest Twitter Moment, showing how far the service has moved beyond its early status as an amplifier of personal minutiae and confession. A minor earthquake had just struck: a magnitude 4.1 temblor centered 45 miles to the southeast. Throughout the Bay Area, thousands of Twitter users seized their smart phones or PCs to peck out 140-character-or-less tweets—updates in the form of text messages, Web-based instant messages, or posts on Twitter's website. Quake-related tidbits coursed through the company's servers at the rate of 296 per minute, according to tracking done by the U.S. Geological Survey.

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The quake was felt more strongly in Mountain View, the site of Google's headquarters—which was metaphorically appropriate. In the first seconds and minutes after the quake, anyone tapping "earthquake Mountain View" (or the name of any other nearby municipality) into Google's search field found that the only hits pertaining to the new quake were ... tweets. While the Google results page included direct information feeds from the USGS and a slick Google Maps display of recent temblors, none reflected the latest event. Official USGS-confirmed data on the quake wouldn't show up until 10:20 A.M. But at 10:12 A.M., the sixth-highest search return was a rolling scroll of tweets posted "seconds ago": *Wow, that was an earthquake jolt in Mountain View!*

The elevation of such observations to the main results page of the Web's dominant search engine was more than just a coming-of-age for the nearly four-year-old service. Twitter's performance as a communication channel during the Mumbai terror attacks in November 2008 and the Iranian election protests last year, its emergence as a political organizing tool during the 2008 U.S. presi-

Photograph by BEN BAKER/REDUX

dential election, and its unexpected role in assorted emergencies (*There's a plane in the Hudson. I'm on the ferry going to pick up the people. Crazy*) had already planted Twitter in the zeitgeist. What the Google hits really represented was the first significant opening of the revenue spigot. Google had recently agreed to pay Twitter for a real-time feed of all tweets; this deal, and a similar and earlier one with the Microsoft search engine Bing, were reportedly worth $25 million combined, making Twitter profitable for the first time. That was big. "I sent a text to Ev the day that we closed

TITANS OF TWEET Twitter founders Evan Williams (far left), Biz Stone (in eyeglasses), and Jack Dorsey (far right) hoist cold ones with Ted Wang, a law partner at Fenwick and West (seated on bar), and venture capitalists Fred Wilson of Union Square Ventures, Bijan Sabet of Spark Capital, and Peter Fenton of Benchmark Capital. The number of Twitter users surged to 75 million last year and the company inked deals worth a reported $25 million with Google and Bing, but its real fortunes depend on proving that tweets have value. "We don't think we are there yet," says Williams. But, he adds, "it's clear there are a lot of ways to make money."

the [Google] deal, and I said, 'I'm going to throw up,'" Stone says. "He texted back, 'I know.'"

With the deals, Google and Bing were acknowledging Twitter's power. The company has helped define a new development: the real-time Web, in which information is generated and consumed almost instantaneously, with social networks, blogs, and other news sources operating in increasingly interlinked ways (CNN Breaking News, for example, has nearly three million followers on Twitter). "Twitter has provided a new building block for the social Web," says Jonathan Zittrain, cofounder of the Berkman Center for Internet and Society at Harvard University *(see "Twitter and the Real-Time Web," p. 56)*. "Amidst the clamor of 'Just had a great bowl of soup' and other trivialities there can be mined some amazing information."

But the question remains: how can a simple technology that's become a crucial part of the Internet be turned into a cash cow? Last September, the company reportedly gained more than $100 million in new funding, atop earlier rounds totaling around $60 million. (Returning investors included Benchmark Capital, Institutional Venture Partners, Union Square Ventures, and Spark Capital; the new players joining them included T. Rowe Price and Insight Venture Partners.) "It definitely feels like there is a shift occurring on the Web—and we think it's a multibillion-dollar opportunity," says Brian Pokorny, a partner with SV Angel in San Francisco, which has invested in Twitter and other companies involved in the real-time Web.

But to make any business model succeed, Williams says, Twitter must keep attracting new users—and prove that tweet-borne information is actually useful. "We are honestly still focused on 'How do we create more value?'" he says. "We have all of this content talking about what's happening in the world right now, and we think there is a lot more value to be gained by users, giving them the right content at the right time. That will lead to advertising and revenue possibilities, but those are completely dependent on people getting value out of it and businesses getting value out of it. But we don't think we are there yet."

The deals with Google and Bing were, therefore, crucial first steps—not only toward bringing in significant revenue but, potentially, toward helping show new legions of users the value of Twitter. Just what Twitter might devise as a business model, however, is impossible to tell, says Randy Komisar, a partner in the venture capital firm Kleiner Perkins Caufield and Byers (which has not invested in Twitter). Will it be keyword-based advertising, sale of market research data, placement of sponsored tweets, or something else? "The speculative game is pointless," he says.

A BILLION TWITTERERS?

Last July, a set of purloined documents laid bare Twitter's agony over how to grow as a business. TechCrunch, a technology-business blog edited by the Silicon Valley gadfly Michael Arrington, posted a remarkable trove of internal Twitter business documents, obtained by a hacker who used a stolen password to enter an employee's Google Apps account. (The TechCrunch posting remains live today.) The documents included meeting notes that captured the angst Twitter felt even as the number of users was skyrocketing, early last year. There was fear that Facebook would coöpt the Twitter model and that Google would "kick our ass at finding the good tweet." The brainstorming was endless: the management team floated ideas from giving away phones preloaded with Twitter to developing a "TV Twitter." They fretted over how to keep employees happy. So much ground was covered that it wasn't possible to discern any one strategy.

But if a single strategy did not surface, grand ambitions did. "What does a completely relevant product look like for a billion people?" one unsigned note wondered. Most striking, the pilfered files included projections that by the end of 2013, not only would Twitter have a billion users, but it would take in $1.5 billion in revenue and $1.1 billion in net earnings—and become "the pulse of the planet." In our interview, Williams would not elaborate. "It's clear there are a lot of ways to make money," he told me. "We want to do it right. We want to do it in a sustainable and scalable way."

Twitter is hardly alone among online social-networking sites in its struggle to find a viable business model *(see "Social Networking Is Not a Business," July/August 2008 and at technologyreview.com)*. As Williams suggests, the path to technology commercialization is rarely an obvious one. It wasn't Google's search technology but its success in selling ads based on keywords that fueled the company's growth. "We always think of these companies as taking a direct line from A to B to C," Komisar says. "But if you look closer, what you see is how crooked the line is that they have to navigate."

Before Twitter's birth nearly four years ago, Williams's big score was his creation of Blogger, a simple-to-use blog hosting service that Google bought in 2003. Blogger was not the original idea but, rather, a by-product of a complex project-management tool for the Web that Williams was trying to develop at a startup called Pyra Labs *(see "What Is He Doing?" November/December 2007 and at technologyreview.com)*. Similarly, Twitter itself was born at Odeo, a Williams-founded startup that was trying to develop a way to distribute podcasts. There, an engineer named Jack Dorsey created a messaging tool—the genesis of Twitter—that he thought would be good for dispatching bike messengers or emergency services. After Apple crushed Odeo's audio ambitions by offering comparable services on iTunes, Dorsey, Williams, and Stone bought the company and eventually spun out Dorsey's tool as Twitter. (Dorsey is now Twitter's chairman; Williams is CEO.)

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Google engineers explain real-time search, and Twitter's founders reflect on the site's popularity:
www.technologyreview.com/realtimesearch

To make any business model succeed, founder Evan Williams says, Twitter must prove that tweet-borne information is actually useful. "We are honestly still focused on 'How do we create more value?'" he says.

And Twitter itself is evolving. Consider the original question a tweet was meant to answer: "What are you doing?" This early emphasis on the personal and the trivial changed as news started to break on Twitter—earning it intense interest from the mainstream media—and as people began using it to network with potential colleagues and keep abreast of the thinking and activities of politicians, stock traders, celebrities. Then users began to redistribute news from media organizations, and the news organizations themselves started to tweet: Twitter became a river of news. The evolution is bound to continue. "Twitter is a tool so basic that it doesn't suggest how you should use it," says Amy Bruckman, a computer scientist at Georgia Tech. "I guarantee that in a few years we will look back at how we used Twitter and laugh."

Indeed, with the help of Twitter's application programming interface (API), which enables outside developers to access its content, constellations of applications and startups have already expanded the service's reach (and some have begun selling advertising). StockTwits, for example, provides an easy way to sift through any tweets that discuss stocks. TweetDeck helps twitterers find categories of tweets to follow. Bit.ly creates shortened versions of Web links that can fit inside tweets. TweetMeme aggregates links found within tweets. Twitpic offers photo distribution. (Most famously, it carried a close-up photo of the US Airways jet adrift in the Hudson, passengers huddled on its wings. The shot was captured by ferry passenger and twitterer Janis Krums.) And so, in November, Twitter ditched "What are you doing?" Now tweets answer the question "What's happening?"

A SHIFTING WEB

The change in Twitter's prompt reflects a shift in the nature of the Web itself. Not only has the medium grown far more social, but online social networks increasingly trade in important real-time information. Adding to the cacophony are proliferating blogs, reports from news organizations, reader comments, and feeds from various other sources. Data feeds, search engines like Google, and easy-to-use widgets—those little on-screen tools that do things like display stock prices or news headlines—can provide instant access to much of this information. "In 2009, we saw this incredible shift of users—and of their attention and focus—to the real-time Web," says John Borthwick, CEO of Betaworks, an Internet media company in New York City that has invested in or launched startups including Bit.ly, TweetDeck, and Summize, a Twitter search tool bought by Twitter in 2008. "It represents a whole new round of innovation, disrupting the way people do the fundamental things they do online." And, he adds, sites like Twitter and Facebook—which has 350 million account holders—are increasingly the first stop for people seeking real-time news.

Of course, that's easy to say—but it's hard to measure and document. Twitter will not share numbers, and third-party measurement of Web audiences has long been dodgy *(see "But Who's Counting?" March/April 2009 and at technologyreview.com*). Measurement is hardest of all with media such as Twitter, because the most common unit of Web usage—page views—doesn't really apply. Tweets, after all, aren't pages; they're the units that make up data streams moving across many platforms and being consumed in myriad ways. As people spend less time on pages and more time sampling streams of data, tracking their behavior becomes extremely difficult. "The majority of what goes on with Twitter doesn't happen on our website," Williams says. "Quantifying Twitter is really hard. That is part of why we don't share numbers, because they are always misleading. We are getting better at it, but it kind of drives us crazy." Still, one proxy—Web-address shortening—gives a sense of how much Twitter and the real-time Web have grown. The number of times people clicked on Bit.ly addresses to open them exploded last year; in December, people did this nearly 2.3 billion times.

In this evolving world, Twitter stands out in many ways. In contrast to communications within many online social networks, tweets by their very nature aim to report something to the world at large. (Facebook posts have long been private by default, but the company is trying to encourage more public posts through changes in its privacy settings.) RJMetrics, a business analytics firm in Camden, NJ, estimates that Twitter has 75 million accounts and that 15 million are responsible for most traffic. Though Facebook's membership dwarfs those figures, "in terms of relative availability of data, Twitter is number one with a bullet," says Eric Marcoullier, a cofounder of Gnip, a company based in Boulder, CO, that aggregates available information from sites like Facebook, Twitter, and Digg for other websites and companies.

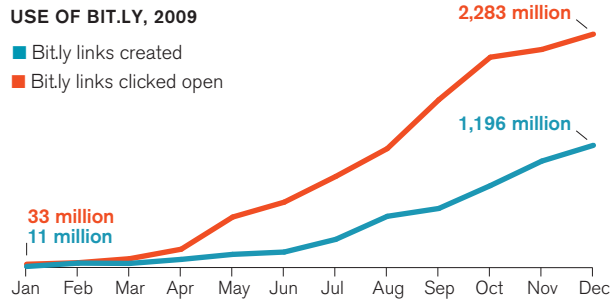
As a result, Twitter has "enormous opportunities" to sell data for commercial use, says Brad Feld, a managing director at the venture capital firm Foundry Group, also in Boulder, CO (it is not a Twitter investor). A local restaurant might want to be notified if Twitterers are saying something negative; Toyota might want data on mentions of its products—as well as competitors' products—to adjust a sales pitch or a product feature. Packaging and providing

TWITTER AND THE REAL-TIME WEB

On the real-time Web, information is created and consumed instantly, often through blogs and social networks such as Twitter and Facebook. The phenomenon exploded last year, as the surging use of URL-shortening services indicates; Web addresses must be shrunk in order for links to fit inside 140-character tweets. Twitter attracted new users and expanded its reach, but it still carries a lot of babble.

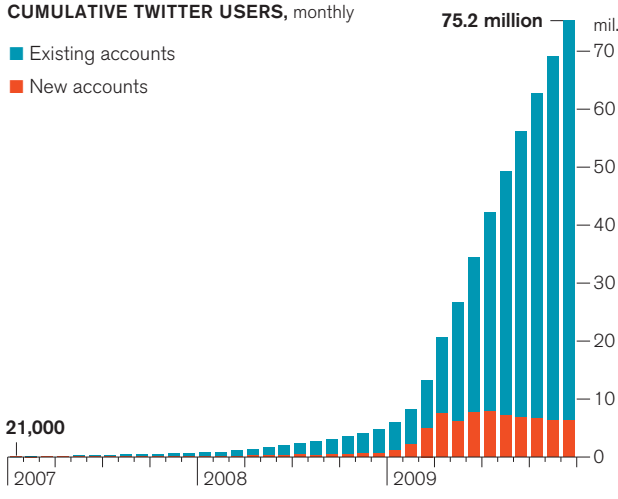
Bit.ly, the leading service for Web-address shortening, experienced nearly 1,000-fold growth last year. In December, people clicked open Bit.ly-shortened addresses nearly 2.3 billion times.

USE OF BIT.LY, 2009



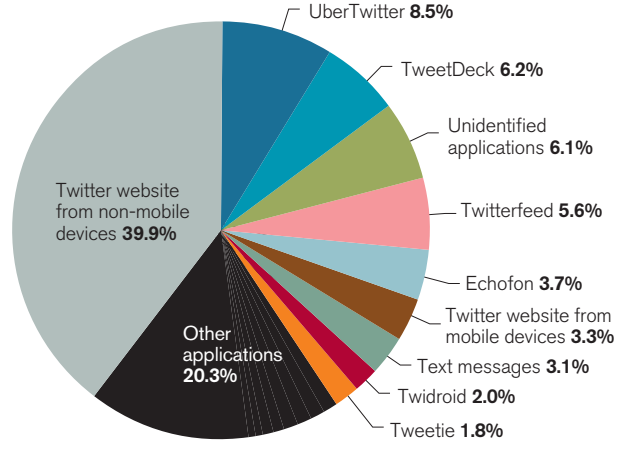
Twitter has experienced exponential user growth in three years. But the rate slowed at the end of 2009.

CUMULATIVE TWITTER USERS, monthly



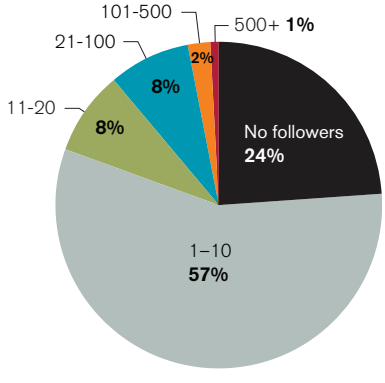
A growing number of tweets come from applications running on other websites. Relatively few are sent as text messages.

PERCENT OF TWEETS FROM TOP SOURCES, December 2009



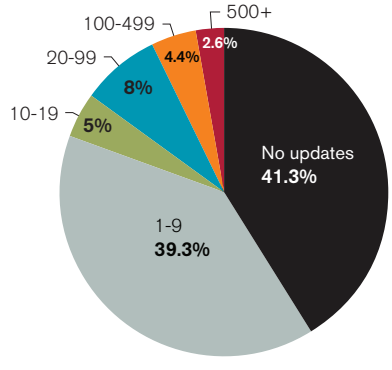
Despite growth, many Twitter users aren't very active. Most have few followers ...

USERS BY FOLLOWER COUNT



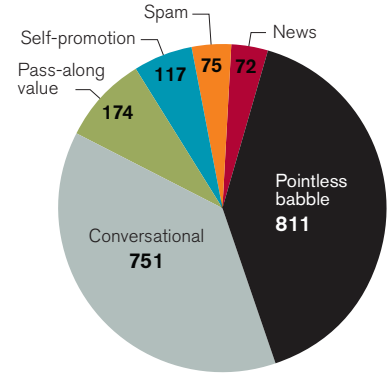
... and aren't doing much tweeting.

USERS BY NUMBER OF TWEETS



And one study of 2,000 U.S. tweets found that much content is of limited use.

CONTENTS OF TWEETS



Sources: Betaworks (Bit.ly); RJMetrics (Twitter data except "Contents of Tweets"); Pear Analytics ("Contents of Tweets")

TOMMY McCALL

such data, for a fee, is clearly something Twitter could start doing, Feld says. He adds that the company could eventually sell keyword-based ads as well.

TWEET RANK

Though Twitter aspires to be the planet's pulse, its own physiology is a bit weak in some areas. The company has no apparent ownership rights to the basic technology for microblogging; its only real assets are its brand and user base. And while Twitter data in theory should be salable to companies, the marketplace is still skeptical. A recent survey by Kognito, a business intelligence firm, found that only 14 percent of market research companies surveyed had immediate plans to mine social-networking data at all.

Twitter needs to win more eyeballs, motivate users to tweet more, and make sure the most useful tweets reach people who might benefit from them. The company understands this. "We are coming out of a year, 2009, which was really about scaling up," Williams says. "We've gotten really good about getting [employees] in here and showing that there is interesting scale to work with here. Just like people who are thinking about *using* Twitter, people coming to *work* at Twitter thought it was some trivial thing—'What are you having for lunch?'—not a global real-time way of finding out what is happening right now. As people learn that it fills a role we actually need filled, we will attract more engineering talent and more users."

The deals with Google and Bing made Twitter profitable. But they are also a means to another end: Twitter skeptics might well be won over if their Web searches start turning up useful tweets. By the same token, a tweet that lands high in Web search results will encourage the person who sent it to keep making timely and useful observations, says Dan Weld, a computer scientist at the University of Washington, Seattle. "When people are able to search tweets more effectively, it will change the content," he says. "People's behavior will be affected. But this will require real-time distribution and highly effective search."

Making real-time search effective is tricky, though. It's not enough just to give searchers the newest tweets that happen to contain a requested keyword. The reputation of the twitterer means something; if you want fresh information about the Haiti earthquake, for example, you'd like to hear it from responsible sources, not just from anyone who happened to include the word *Haiti* in a tweet. As a first step, Google evaluates tweets in part with a technological analogue to its PageRank technology, which analyzes the link structure of Web pages to judge their relevance. Generally speaking, the more links to a page—and the more pages linked to the linkers—the more relevant Google's search engine considers it. Similarly, Google concludes that the more people who "follow" a Twitter user—and the more people who follow *those* people—the more credible and relevant his or her tweets probably are.

But such efforts are only the beginning. Consider a real-time search for "iPod." An engineer doing such a search might be seeking insights into its software, a high-school student might be most interested in friends' opinions or whether the gadget's retail price has dropped, and a music executive might want to look for trends in what kinds of music people are downloading. Finding out what specific people want might require some analysis of their social networks, their past tweets, and the tweets of the people they follow, says Eugene Agichtein, a computer scientist at Emory University who is doing research on social search.

The location from which a tweet was issued can be an enormous help. Messages from mobile devices with GPS receivers can include location information. Twitter began allowing such information to be attached to tweets last summer, and Google and others are exploring ways to use this data to provide more relevant real-time results. "If you follow me and know that I work in Mountain View or live in Menlo Park, you just assume that when I publish something—'*I saw five fire engines*'—you know it's in the general Bay Area," says Dylan Casey, Google's product manager for real-time search. "But that comment would become even more powerful if you knew the exact geolocation."

Twitter itself recently refined its home page's "Trending Topics" feature—a compendium of the most common phrases appearing in messages—to allow twitterers to see what subjects are being discussed where they live. (Twitter determines the location partly on the basis of twitterers' IP addresses or their reported home cities.) The new feature, called "Local Trends," is the next logical step in making real-time search more relevant and interesting. "Search isn't just a box and a button; it's about serendipity," Williams says. "It's about hopefully, and ideally, surfacing information to you that you, as a twitterer, didn't ask for, but wanted—and right at that moment. In the world of real-time search, the Holy Grail is that you anticipate what the user wanted. Our opportunity and challenge is solving that problem—thinking of how users behave in the ecosystem. It gets you much quicker to realizing the value of Twitter."

There is no one magical algorithm that provides serendipity without spam, relevance without rubbish, to all people in all places. But Twitter and other companies see tremendous opportunities in the ocean of tweets—and, more generally, in mining the social Web for information that people want. "What's really important here is the notion of the social Web and using your social network—people that you trust—for information discovery," says Feld. "We've got a long way to go here, which is really exciting for any entrepreneur playing in this domain." Even if the future business model of Twitter is not certain, the fast-changing nature of the Web itself provides evidence enough that one will emerge—and might even represent the next seismic shift in the Internet industry. TR

DAVID TALBOT IS *TECHNOLOGY REVIEW*'S CHIEF CORRESPONDENT.

Turning Math into Cash

IBM has found a new source of revenue: using its mathematicians' formulas in business services.

By WILLIAM M. BULKELEY

Five years ago, Brenda Dietrich started to investigate how IBM's 40,000 salespeople could learn to rely a little more on math than on their gut instincts. In particular, Dietrich, who heads the company's 200-person worldwide team of math researchers, was asked to see if math could help managers do a better job of setting sales quotas. She assigned three mathematicians at IBM's Thomas J. Watson Research Center in Yorktown Heights, NY, to work on new techniques for predicting how much business the company could get from a given customer.

The mathematicians collected several years' worth of data about every sale IBM made around the world. They compared the results with the sales quotas set at the beginning of the year, most of which were developed by district sales managers who negotiated them with sales teams on the basis of past experience. To spot opportunities the sales teams didn't recognize, the researchers collected external data on IT spending patterns by industry and combined that information with the internal sales data. Then they used a technique called high-quantile modeling—which tries to predict, say, the 90th percentile of a distribution rather than the mean—to estimate *potential* spending by each customer and calculate how much of that demand IBM could fulfill.

50 PAGE 37

Armed with these predictions about how much equipment IBM should be able to sell to each customer, Dietrich's mathematicians looked at the size and makeup of the sales team on each account and compared its actual performance with the theoretical maximum. Some teams were so small they couldn't sell enough to meet that potential demand. Other teams were unnecessarily large. So the mathematicians advised the sales department to shift its staff around, taking less productive salespeople off the big teams and putting them on teams that had been too small. Sales in the latter accounts quickly grew.

The two-year project had a tremendous payoff for IBM. The corporate controller concluded that it generated $1 billion in additional sales through 2008, the year after the team finished its work, says Dietrich, a 50-year-old PhD with a sneaking suspicion that the world would work better if it were run by mathematicians. Since then, IBM has incorporated high-quantile modeling into its workforce analytics practice, a service it offers to help clients make decisions about human-resources issues such as how best to deploy their salespeople.

And the company drew a more general lesson from the experience: it came to believe that its mathematicians' innovations were something for which other businesses would pay handsomely. Last year, the company created a major new business analytics and optimization group within IBM Global Business Services, and the group has already trained 4,000 consultants. IBM hopes to eventually do as much business in analytics as it already does in enterprise resource planning, which helps companies coördinate their information technology across separate departments; that service is a leading source of revenue in the $17.7 billion business services unit and has been one of its fastest-growing areas over the last 10 years. The two groups already complement each other: while enterprise resource planning tracks and organizes business processes, analytics maximizes their performance.

Photograph by HEATHER JOHNSON

MATH MAGICIAN
At IBM's Watson Research Center, Brenda Dietrich helps connect the work of the company's research mathematicians to its consultants' projects, generating enormous amounts of new business.

Dietrich, whose name is on 13 patents, thinks she and her team can create models that accurately describe activities far outside what is normally considered the realm of mathematics. For example, stochastic optimization algorithms, which incorporate random elements rather than assuming that all values are exact, have been used for decades to help manufacturers and financial markets adjust to changing conditions. But IBM's mathematicians are applying the techniques to problems in human resources and marketing. They are using mathematical models to help the company find new customers and figure out the right mix of veteran and junior programmers to assign to a big software project. They are analyzing data to determine whether it is worthwhile for IBM to advertise in specific magazines or on certain television shows, or to attend particular trade shows. "We're able to predict the impact of certain advertising programs on revenues," Dietrich says—though, she concedes, "not with the precision I would like."

Even if they are imprecise, Dietrich believes, these analytic techniques can be hugely helpful to many companies, which she says often don't fully understand their internal processes and business models. Studying all the available data about sales and manufacturing could reveal bottlenecks that might be cleared or uncover opportunities that have been missed. She and her team are increasingly getting involved directly with customers. For instance, because of her reputation as a scientist and head of a math research team, she was recently invited to talk to a big pharmaceutical company's executives about whether mathematical modeling could improve their process for allocating funds to various drug development efforts.

Such activities are a big departure from what IBM mathematicians used to do. In the old days, they were an odd breed among the scientists and engineers, who worked on science and technologies that might eventually lead to new semiconductor materials, new storage devices, or parallel-processing supercomputers. The mathematicians sometimes modeled IBM production processes, but they were judged mostly by their theoretical work and their publications in academic journals.

That started to change in the early 1990s, when IBM racked up huge losses. The board pushed out top management and brought in Louis Gerstner, then the head of RJR Nabisco, to serve as CEO. Though Gerstner took steps to break up IBM's sclerotic bureaucracy, he chose to keep the company in one piece. He said he believed that IBM's size, which enabled it to focus resources on big problems for large corporate and government customers, was a valuable asset that should be preserved.

A key part of Gerstner's strategy was to unify and expand IBM's global-services business. Paul Horn, who headed IBM Research during part of that time and is now senior vice provost for research at New York University, saw that under the circumstances, the labs could easily be viewed as a costly luxury. With services growing, he says, "if research wasn't contributing, you could imagine someone in the future saying, 'You don't need to be so big.'" Horn, a physicist, helped convince Gerstner that IBM's research division could play an important role in his strategy by working with customers to solve their problems. He began pushing his thousands of researchers, including the mathematicians, to start working on projects that could be useful to the services business. The motive was simple, he says: "Survival."

For the mathematicians, the shift was a natural one. Dietrich says they had frequently worked with IBM's own manufacturing plants on scheduling problems and logistical issues, though the results were usually considered proprietary. And they had already begun getting more involved in business operations, in part because it provided them with the large data sets that they needed for modeling. Historically, stochastic optimization had been limited by the sheer amount of computing required to deal with multiple variables. But as computer power exploded and researchers began to use massively parallel processors, they were able to manipulate much more data.

IBM Research mathematician Baruch Schieber recalls going to a Brazilian steel mill and finding that production schedules were being drawn up on whiteboards. Surely, mathematical models could do it better, he thought. He was especially interested in the issues involved in scheduling production runs for different varieties of steel. Though it's cheaper to do long runs of one type of steel, sometimes customers need several different types immediately, so the mill has to do short runs. "Mathematical modeling is quantifying things that usually aren't quantified," he says—such as the tradeoff between cost and customer satisfaction. Early in a contract period, Schieber discovered, the mills wanted to optimize their schedules for maximum efficiency and minimum cost. At the end of the period, when the contract was up for renewal, they sought to focus more on improving satisfaction. Similar issues arise with airlines. Schieber says, "We ask managers: do you want to minimize crew costs or fuel, or do you want to maximize customer satisfaction?"

William Pulleyblank, who headed IBM's math department in the 1990s, had urged the company even then to make a business out of analytics. "A lot of companies tried to do this," he says. "It was seen as a pure product play—package it and sell it." However, he adds, it became clear that IBM didn't have a good way to sell the mathematicians' skills to clients. He concluded that many companies' needs were so specialized that designing a general-purpose software package wouldn't be profitable—but software designed for particular businesses wouldn't be in high enough

www Brenda Dietrich explains how to use math to increase revenues: **technologyreview.com/ibm**

Some businesspeople worry that depending on analytics will make leaders indecisive when they don't have an abundance of data. But Dietrich is more concerned that companies will fail to analyze the petabytes of data they do collect.

demand. At the same time, IBM didn't want its researchers to become consultants. The mathematicians didn't want to do it, and they weren't trained for relating to customers. "I realized the challenge wasn't the math," says Pulleyblank, who is now a vice president in the business analytics and optimization group. "It was how to make it a business."

The path to an analytics business became clearer in 2002, when IBM paid $3.9 billion to acquire the consulting business of PricewaterhouseCoopers. Ginni Rometty, who spearheaded the deal and now heads IBM's sales operations, recalled Pulleyblank's idea. She thought that PWC's consultants could expand IBM's service offerings beyond IT; its researchers could be touted as a unique source of advice to client companies on marketing, human resources, and logistics. Each fall, when IBM's sales teams start forecasting upcoming business, the consultants identify critical problems that are likely to affect particular industries in the coming year. If those problems look like analytics issues, the consultants contact the business analytics and optimization team and ask whether IBM has worked on anything similar before. In many cases, the problems can indeed be addressed by adapting the company's existing software products.

When existing software can't do the job, the consultants turn to IBM Research for help. Sanjeev Nagrath, IBM's global leader for supply-chain management, encountered such a situation last year when clients started asking how to reduce the carbon footprint of their supply chains. So, Nagrath says, they're working with Research to come up with industry-specific models to deal with sustainability issues. And two years ago he worked with Dietrich to create a center for supply-chain innovation in Beijing. There, Chinese mathematicians are part of a team working with companies such as Chinese shipping giant Cosco. The innovation center's mathematicians helped IBM consultants model Cosco's procedures and developed a plan that cut fuel costs 25 percent and carbon dioxide emissions 15 percent. Among other things, they recommended reducing the number of distribution centers from 100 to 40.

Not all clients trust the mathematicians' contributions, as Schieber found out when he created a model that could be used to reschedule ships if supplies were temporarily halted by bad weather. He says it was much better than human schedulers at adjusting fleet movements and speeds to minimize disruption and fuel costs. But the customer wasn't satisfied. "It was a black box," he recalls. "The shipper said, this is our competitive edge. They wanted to understand it." The shipping company finally implemented the model after IBM redesigned it so that it was not a fully automated system but an aid that human dispatchers could consult.

Some businesspeople argue that many decisions are best guided by gut reactions based on years of experience. They worry that depending on analytics will make business leaders indecisive when they don't have an abundance of data. And a math-phobic public is suspicious that analytics-driven programs cut costs at consumers' expense. IBM researchers point to the recent backlash against recommendations that annual mammograms be delayed until women are 50 because they don't provide statistically provable benefits for younger women.

But Dietrich is more concerned that companies will fail to analyze the petabytes of data they do collect. When she met with the pharmaceutical company about its portfolio management strategy, for instance, the executives explained how they allocated spending according to their estimates of how likely each project was to succeed. "I asked them if they ever checked to see how well the estimates matched their results," she says. "They never had."

Dietrich and her researchers are now working to rewrite optimization algorithms to take advantage of massively parallel computers. The older programs were written to minimize the number of operations required. But now that thousands of processors can churn through vast data sets, she says, "the issue is to reduce [run] time." Once the team is done, those optimization programs will be available to businesses whose stores of data are too large to be analyzed with single-thread computer programs.

The most interesting problems the mathematicians envision for future projects involve situations where a model must incorporate behavioral changes that the model itself has inspired. For example, Dietrich says, a traffic congestion system might use messages sent to GPS units to direct drivers away from the site of a highway accident. But the model would also have to calculate how many people would take its advice, lest it end up creating a new traffic jam on an alternate route. She says that understanding the way systems change as humans react to incentives is one of the big challenges for mathematical modeling.

Of course, it's never going to be easy to accurately predict what people—or businesses—will do. But thanks to their insights as mathematicians and their access to IBM's vast computing power, Dietrich and her colleagues are getting better at it. And now, other companies are paying for that skill. TR

WILLIAM M. BULKELEY IS A FORMER *WALL STREET JOURNAL* REPORTER WHO IS NOW A FREELANCE WRITER IN BOSTON.

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Career Growth Profile

Foster Hinshaw

Age: 61

Job Title: CEO and President

Employer: Dataupia.

Graduate Programs: MS, engineering, Cornell University, 1971; MBA, Harvard University, 1974

Foster Hinshaw, the founder, CEO, and president of Dataupia, understands the power of information. Through technology, his company helps businesses affordably streamline and quickly access massive amounts of data so they can operate with greater insight and efficiency. It's the perfect challenge for Hinshaw, an enterprising engineer with a head for business.

While some tech industry executives wait until midcareer to earn advanced degrees in business or management, Hinshaw knew as an undergraduate at Cornell University that his schooling should go beyond engineering formulas and equations.

"Apart from engineering, I have always had a strong interest in strategic and nontechnical issues, and I knew I wanted to combine these interests," he says. "I learned from the experiences of my engineering-school classmates that the path out of engineering and into business without an MBA was difficult. To become successful and hone my business skills, it was clear that I would need to further my education outside of engineering with an MBA."

Upon finishing his bachelor's and master's degrees in engineering, Hinshaw applied for and was accepted to the MBA program at Harvard University. Almost every summer during his college years, he worked to pay for his degrees. He started out in tech positions, working at Pan Am as a radio technician and at Hewlett-Packard as an engineer. "The inside knowledge I gained from being on the tech side in those early years of my career definitely deepened my understanding of how to make successful and impactful business decisions in tech-based companies later on," he says.

Armed with an MBA, Hinshaw ventured into the business world in 1974. He has worked almost exclusively with small companies and startups ever since. His first job with a startup was as an engineer for Electric Fuel Propulsion, a manufacturer of full-sized electric cars.

Hinshaw also spent several years as a Y2K practice manager at Keane before moving on to become the chief financial officer and director of information systems for VideoGuide (now part of TV Guide).

To learn more about Foster's decision to continue his education—and how it helped him move up the corporate ladder, visit **www.technologyreview.com/careerresources/.**

Program Directory

BRIEFING

PERSONALIZED MEDICINE

Cheap DNA sequencing will drive a revolution in health care

LEONARD LESSIN / PHOTO RESEARCHERS, INC.

The dream of personalized medicine was one of the driving forces behind the 13-year, $3 billion Human Genome Project. Researchers hoped that once the genetic blueprint was revealed, they could create DNA tests to gauge individuals' risk for conditions like diabetes and cancer, allowing for targeted screening or preëmptive intervention. Genetic information would help doctors select the right drugs to treat disease in a given patient. Such advances would dramatically improve medicine and simultaneously lower costs by eliminating pointless treatments and reducing adverse drug reactions.

Delivering on these promises has been an uphill struggle. Some diseases, like Huntington's, are caused by mutations in a single gene. But for the most part, when our risk of developing a given condition depends on multiple genes, identifying them is difficult. Even when the genes linked to a condition *are* identified, using that knowledge to select treatments has proved tough *(see "Drowning in Data," p. 65)*. We now have the 1.0 version of personalized medicine, in which relatively simple genetic tests can provide information on whether one patient will benefit from a certain cancer drug or how big a dose of blood thinner another should receive. But there are signs that personalized medicine will soon get more sophisticated. Ever cheaper genetic sequencing means that researchers are getting more and more genomic information, from which they can tease out subtle genetic variations that explain why two otherwise similar people can have very different medical destinies. Within the next few years, it will become cheaper to have your genome sequenced than to get an MRI *(see "A Moore's Law for Genetics," p. 68)*. Figuring out how to use that information to improve your medical care is personalized medicine's next great challenge. —*Stephen Cass*

This DNA sequencing machine from Illumina is capable of reading over five billion bases per day.

TECHNOLOGY OVERVIEW

Faster Tools to Scrutinize the Genome

The majority of genetic diagnostic testing is done with sequencing, which identifies each base, or "letter," in a string of DNA. Sequencing can be used to identify all of the roughly three billion base pairs in a human genome, but most clinical testing is limited to sequencing single genes, which can reveal the presence of a mutation that could result in a disease or other disorder. In research, scientists use newer techniques that can scan millions of strands of DNA in parallel—a faster, cheaper process that provides vast amounts of genetic data. But these advanced sequencing tests have yet to be approved or optimized for the practice of medicine.

Most of the fast new sequencing technologies, developed by Illumina, Applied Biosystems, Complete Genomics, and others, use a camera to record fluorescently labeled bases as they bind to bits of a target sample of DNA. Watching a series of these reactions enables software to piece together the DNA sequence. Each company has developed novel ways to densely pack short strands of DNA onto a chip or slide, allowing millions of reactions to be recorded at once *(see "Complete Genomics," p. 67)*. Most techniques require DNA molecules to be amplified, or copied many times before sequencing, but even newer methods such as those being developed by Pacific Biosciences and Oxford Nanopore can read the sequence of a single molecule, making it simpler to prepare samples and piece together the sequence.

Another way to scrutinize DNA uses microarrays, chiplike devices that, instead of reading the DNA sequence letter by letter, spot genetic variants known as single-nucleotide polymorphisms (SNPs). Microarrays provide a fast and effective way of screening for a particular variant or pattern of SNPs. Microarray studies have identified hundreds of SNPs that are linked to common diseases. But for the most part, the results have yet to translate into clinical practice. Because such mutations account for only a small percentage of an individual's overall risk of disease, scientists haven't yet figured out how to use this information to improve health *(see "Drowning in Data," opposite)*. Researchers are also developing tests for proteins and other biomarkers that reflect how an individuals' genes interact with the environment.

To date, most advances in personalized medicine have occurred in cancer. For example, genetic screens that sequence portions of genes linked to breast cancer have been available to women with a family history of the disease for over a decade, so that those who carry high-risk variants can be monitored aggressively. Drug makers and scientists have also found genetic markers that predict whether a patient will respond to a given cancer drug, and a few new drugs require accompanying diagnostic tests that use sequencing or microarray technology to profile these markers *(see "FDA Takes On Personalized Medicine," p. 69)*.

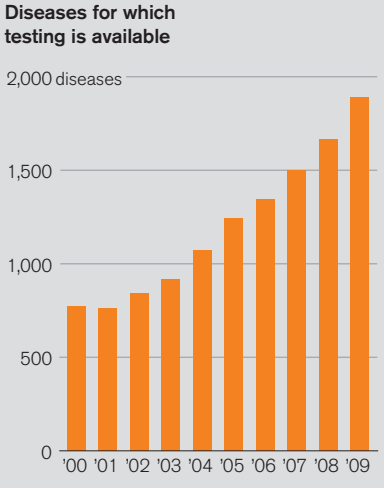
But so-called pharmacogenetic testing is still limited, especially beyond cancer drugs, not least because most genetic

WWW See an interactive graphic mapping diseases to the human genome: **www.technologyreview.com/briefings/personalmed**

ILLUMINA

TEST EXPLOSION

The number of genetic tests available for clinical and research purposes is rapidly increasing.



Source: NCBI

testing must be done in specialized labs and can take weeks. In order to personalize a prescription for someone who has suffered a heart attack, a physician needs information while the patient is still in the hospital. A number of companies are developing desktop devices for use in hospitals, using microarrays that can determine from a drop of blood whether a patient is likely to respond well to a drug. But to truly fulfill the promise of personalized medicine, the advanced sequencing methods in development will need to extend further into clinical practice, making it as easy to read patients' DNA as it is to send them for x-rays or cholesterol tests. *—Emily Singer*

DATA SHOT

3,669

The number of genes currently known to be associated with diseases, out of an estimated total of 20,000 to 25,000.

MONTY RAKUSEN/GETTY IMAGES

INDUSTRY CHALLENGES

Drowning in Data

The personalized-medicine industry aims to convert information about an individual's genome into useful diagnostic tests and targeted drug treatments. Companies that deal with gathering the information—sequencing genomes and identifying genetic variations—have made impressive technical advances that have dramatically reduced the cost of analyzing DNA *(see "Faster Tools to Scrutinize the Genome," opposite)*. Now the biggest challenge lies in interpreting the huge volume of genetic data being generated. Studies have identified thousands of candidates for genes underlying common diseases, for example, but it's not clear how to make that information medically useful.

The problem is going to get worse before it gets better. Most genetic variation discovered to date accounts for a fairly small percentage of the overall risk of disease. Countless genetic variations are still hidden in our genomes. As scientists begin to uncover the remaining genetic culprits, they will need to develop ways to interpret what those variations mean for individual health. "The field urgently needs a breakthrough in the way we analyze such data, or we will end up with a collection of data … unable to predict anything," wrote Serge Koscielny, a researcher at the National Institute of Health and Medical Research in Villejuif, France, in the journal *Science Translational Medicine* in January.

Efforts to find solutions are just beginning. Personal-genomics companies such as 23andMe and Navigenics have developed their own algorithms for combining

Digital sequencing systems can capture vast amounts of genetic data, but interpretation has been difficult.

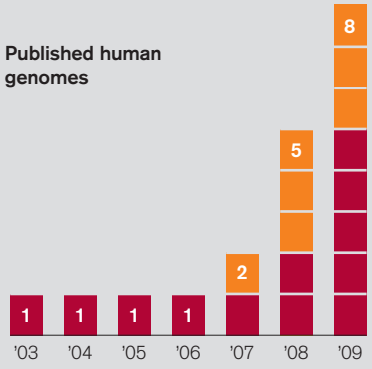
different genetic risk factors into a predictive risk score. And Knome, a personal-sequencing startup based in Cambridge, MA, is taking this strategy one step further by developing software to analyze entire genome sequences. But it will be impossible to develop effective analysis methods—or weigh their predictive power—without large databases that pair individuals' genome sequences with their medical records.

Genetic tests and therapeutics also face an economic challenge: who will pay for them? Insurance companies will not cover these diagnostics unless they are proved to be both effective—accurately spotting whether a person will respond to a drug, for example—and cost-effective. Insurers would be motivated to pay for tests that could rule out an expensive cancer treatment as unlikely to work. But with drugs that are inexpensive in the first place, the financial case for such testing is less obvious.

If scientists succeed in developing tests that can accurately predict an individual's risk of disease years or decades in advance of symptoms, the problem of who pays will become even trickier—especially in the United States, where people change insurance plans every three to four years on average. Pharmacy benefits managers such as Medco and CVS Caremark, which provide prescription-drug coverage to many Americans on behalf of employers and insurers, are starting to take the lead in judging the economic value of personalized medicine *(see "Sequencing Companies Dominate Investment," p. 70)*. *—Emily Singer*

GENOME GENESIS

More and more people will have their genomes sequenced as the process becomes faster and cheaper.



DATA SHOT

24

The number of genes that could be linked to autism, according to a computational analysis conducted by Columbia University researchers. The analysis also suggested 21 genes that could be implicated in bipolar disorder and 25 in schizophrenia.

TABLES

Drugs with Pharmacogenomic Tests

Drug	Purpose	The gene factor
Atomoxetine HCl (Strattera)	ADHD treatment	Patients with a mutation in the *CYP2D6* gene are at risk of suffering serious liver damage.
Clopidogrel (Plavix)	Prevents heart attacks by inhibiting blood clots	A variation of the *CYP2C19* gene interferes with the way the drug is metabolized, rendering it ineffective.
Cetuximab (Erbitux) and Panitumumab (Vectibix)	Colorectal cancer drug	The drugs work only in people whose tumors have a normal *KRAS* gene.
Gefitinib (Iressa)	Lung cancer drug	Works best on people whose tumors have a mutation in the *EGFR* gene.
Irinotecan (Camptosar)	Colorectal cancer drug	People with a genetic variant suffer side effects because they have fewer liver enzymes to break down the drug.
Tamoxifen (Nolvadex)	Breast cancer drug	Variations in the *CYP2D6* gene can make a person metabolize the drug too quickly or not at all.
Warfarin (Coumadin)	Blood thinner	In patients with either or both of two genetic variations, the drug can cause excessive bleeding rather than help prevent blood clots. Genetic testing can reveal the right dose.

CASE STUDY

Complete Genomics: Fast, Cheap Sequencing Service

Companies are struggling to make it fast, affordable, and profitable to sequence individuals' genomes—a tall order considering that until late 2008, fewer than 10 human genomes had been sequenced, and those at considerable expense. Four-year-old startup Complete Genomics, based in Mountain View, CA, thinks it has cracked the problem. It demonstrated its technology by sequencing what it claims were more than 50 genomes in 2009. Now it is scaling up its facility to sequence, it says, as many as 5,000 individual genomes in 2010, with 10,000 genomes a year thereafter, at $1,500 to $5,000 each.

The key to the company's technology is the ability to analyze more than a billion amplified particles of DNA on a single microscope slide. Putting so much information on a single array reduces the number of slides and the amount of expensive reagent required to sequence a genome, and it speeds up digital imaging. Rather than selling its sequencing technology in the form of machines, reagents, and software, as its competitors do, Complete Genomics sells sequencing as a service, taking orders from researchers who FedEx samples to the company—eight genomes minimum, no maximum. "That's a very easy business to scale up quite rapidly," says CEO Clifford Reid.

For now, the company is taking advantage of the pent-up demand for sequencing among researchers, who have already placed orders ranging from tens to hundreds of genomes. After the initial research rush passes, Complete Genomics hopes to enter consumer and medical markets. The continuing drop in prices *(see "A Moore's Law for Genetics," p. 68)* leads some experts to predict that soon the genome of every newborn will be sequenced at birth. That's more than four million genomes per year in the United States alone. And most oncology researchers believe that sequencing the DNA of a patient's tumor will one day be the key to effective treatment. Because every cancer seems to have its own set of mutations, its entire genome will be sequenced as if it were a person.

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Given the potential demand, Reid is bullish. He says, "We expect to open 10 sequencing centers around the world that, collectively, will have the ability to sequence one million genomes over the next five years." *—Lauren Gravitz*

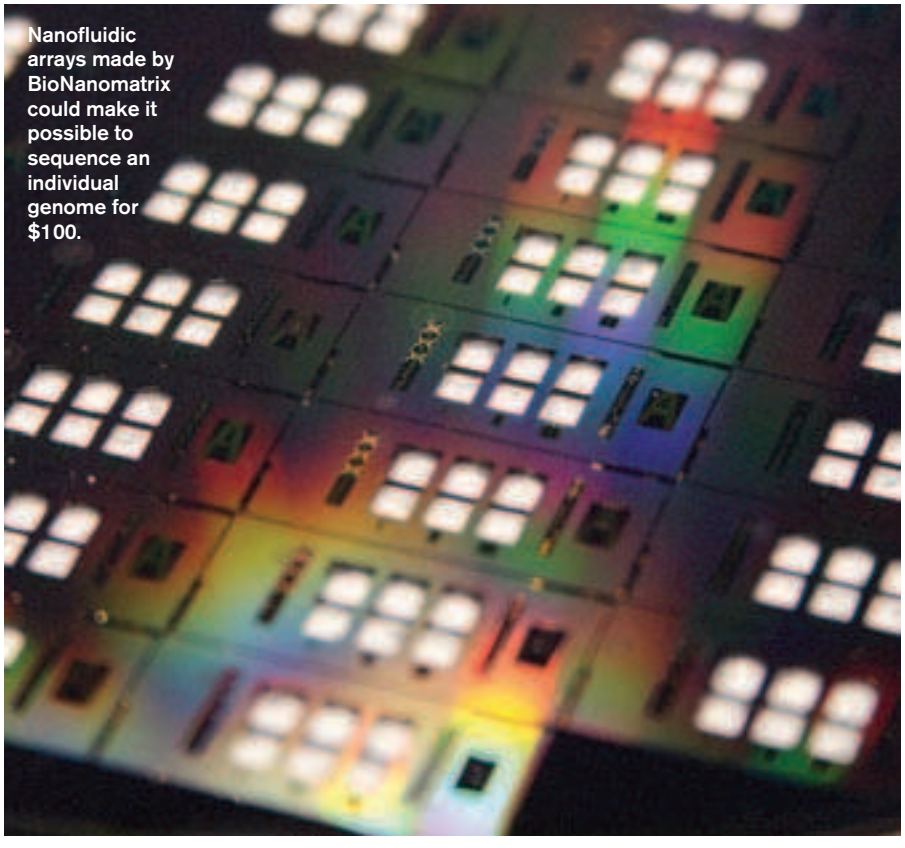
Complete Genomics is building a facility full of automated sequencing instruments like this one.

JEN SISKA

DATA SHOT

778
megabytes

The size of one human genome, stored in a standard format that uses two bits to specify each base in the DNA sequence. The human genome contains about three billion base pairs.



Nanofluidic arrays made by BioNanomatrix could make it possible to sequence an individual genome for $100.

OVER THE HORIZON

A Moore's Law for Genetics

Sequencing the first human genome cost $3 billion—and it wasn't actually the genome of a single individual but a composite "everyman" assembled from the DNA of several volunteers. If personalized medicine is to reach its full potential, doctors and researchers need the ability to study an individual's genome without spending an astronomical sum. Fortunately, sequencing costs have plummeted in the last few years, and now the race is on to see who can deliver the first $1,000 genome—cheap enough to put the cost of sequencing all of an individual's DNA on a par with many routine medical tests.

Interpreting genomic information is still a very difficult task *(see "Drowning in Data," p. 65)*, and we have limited knowledge of how genetic variation affects health. But people will still want to get sequenced, suggests George Church, a geneticist at Harvard Medical School and a pioneer in sequencing technology: he says there are 1,500 genes that are considered "medically predictive" and for whose effects mitigating action is possible. A once-in-a-lifetime test could reveal, for example, whether someone couldn't metabolize a particular drug or should pay careful attention to diet and exercise because of a propensity for heart disease. The $1,000 barrier is expected to be broken in the next year or two, with even cheaper sequencing to follow.

"The key thing that's driving all of the next-generation sequencing is miniaturization," says Church. Just as miniaturization steadily decreased the price of computer chips, genome sequencing is getting cheaper as working components are shrunk down and packed more densely together.

Advances include using microfluidics to reduce the volume of chemicals needed for analysis, which saves money because reagents are responsible for a large fraction of sequencing cost. In addition, some companies, such as BioNanomatrix, are developing tiny nanofluidic devices that force molecules along channels about 50 nanometers wide. The company says that using such channels could bring the price of sequencing down to $100 per genome—though it will probably be at least five years before that happens. *—Courtney Humphries*

BIONANOMATRIX

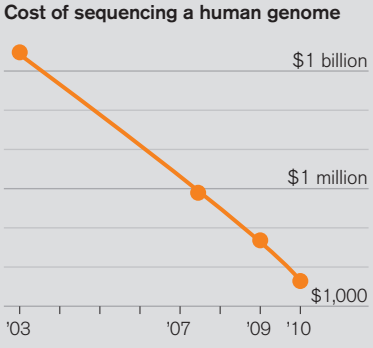
DATA SHOT

60 to 90

The number of days it takes to get a genome sequenced by Illumina's service, which costs $48,000. The first human genome sequence took 13 years.

GOING DOWN

An exponential decrease in the cost of sequencing DNA could soon result in a $1,000 genome.



POLICY

FDA Takes On Personalized Medicine

Personalized medicine does not fit easily into established government procedures for approving drugs. After all, clinical trials are designed to test a drug on a large and diverse group of patients, and the whole point of personalized therapeutics is to target the specific genetic populations that will benefit most. The U.S. Food and Drug Administration is now trying to figure out how to judge the usefulness of a drug designed for particular genetic groups while also considering its safety for others who may receive it for off-label purposes.

Last fall the FDA created a post for a genomics advisor, who will coördinate the agency's efforts to address the subject of genetic data and prescription drugs. Amy Miller, public-policy director of the nonprofit Personalized Medicine Coalition, says the agency has signaled that it's "now ready to give the industry some guidance on how personalized-medicine products will be regulated in the future."

One of the first challenges the FDA will probably tackle is how to evaluate genetic and biomarker-based tests aimed at identifying the patients most likely to benefit from a drug. The agency has begun adding recommendations for diagnostic tests to drug labels, and in a handful of cases it has mandated a genetic test before a drug can be prescribed, but there is currently no streamlined path for approving the combination of a drug and a diagnostic test. The FDA has indicated that it will develop guidelines, but so far it's not clear how, or when, it will resolve the logistical difficulties involved in approving two very different products in one regulatory process. —*Courtney Humphries*

The FDA recommends genetic testing before patients are given prescriptions for Erbitux, a treatment for colorectal cancer.

BRISTOL MYERS SQUIB

TABLES

Personal Genomics

Company	Technology and cost	You get information about …
23andMe Mountain View, CA	Microarrays that test for genetic variations $399 to $499	Ancestry, disease risk, carrier status, and sensitivity to particular drugs
deCode Genetics Reykjavik, Iceland	Microarrays that test for genetic variations $195 to $985	Ancestry and genetic susceptibility to diseases such as various cancers
DNA Direct San Francisco, CA	Varies by subcontractor $175 to $3,456	Risk for more than a dozen conditions, including cystic fibrosis and breast cancer
Knome Cambridge, MA	Complete genome sequencing $68,500	Your entire genome sequence (analysis by a team of scientists is included)
Navigenics Redwood Shores, CA	Microarrays that test for genetic variations $999	Genetic predisposition to dozens of diseases, including Alzheimer's, type 2 diabetes, and various cancers
Pathway Genomics San Diego, CA	Multiple platforms to test for genetic variations $199 to $399	Risks for up to 90 conditions; information on ancestry, carrier status, and drug sensitivities

MARKETWATCH

Sequencing Companies Dominate Investment

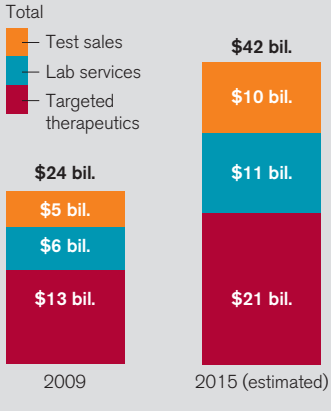
The market for personalized medicine is growing: according to PricewaterhouseCoopers, the core market will reach $42 billion by 2015. However, that growth is not uniform. Some areas, such as genomic sequencing, are surging ahead; others, such as translating genetic data into clinically useful information, languish.

In this environment, startups developing sequencing technologies, such as Pacific Biosciences, Illumina, and Complete Genomics, have attracted sustained investor interest as they race to create ever cheaper ways to decode DNA *(see "Faster Tools to Scrutinize the Genome," p. 64)*. In their most recent rounds of venture funding last summer, Pacific Biosciences and Complete Genomics received $68 million and $45 million, respectively.

EXPANDING ECONOMY

Core sectors of the personalized-medicine industry will experience significant growth in the next few years.

Growth in personalized medicine market



Source: PricewaterhouseCoopers

Diagnostic technologies, too, are moving at a rapid pace. Startups from Boston to Silicon Valley have been pinning down disease-related genetic markers and creating many new tests that are already in the clinic or on their way. As these companies grow and bring more tests to market, large diagnostics companies are likely to acquire them, says venture capitalist Brook Byers of Kleiner Perkins Caufield and Byers.

One of the biggest undeveloped areas in personalized medicine, however, is the information technology needed to analyze and store the huge quantity of genetic data that is starting to pour forth *(see "Drowning in Data," p. 65)*. Of the few bioinformatics companies working to digest the data, Proventys, based in Newton, MA, is among the furthest along. Its technology combines biomarkers and other information to make risk predictions about diseases.

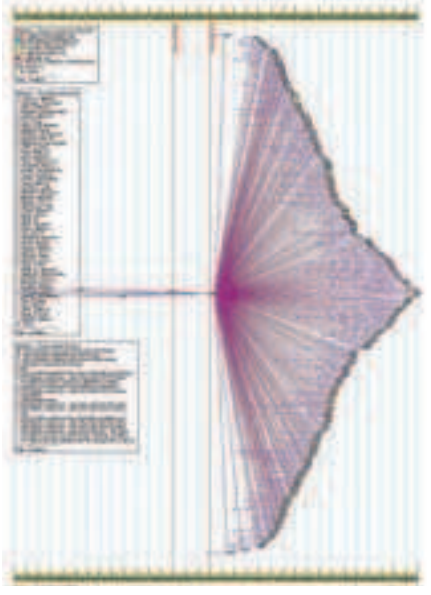
Meanwhile, pharmaceutical companies are responding to the nascent market for personalized therapeutics in different ways. Pfizer, for example, is collaborating with existing biotech companies to develop drugs and diagnostics based on genetic testing. AstraZeneca recently announced a partnership with the Danish diagnostics company Dako, the first of many alliances it plans in a strategy for bringing genetic tests to market. Novartis is taking a different tack, dedicating a large portion of its own resources to developing personalized medicine.

In the United States, benefit management companies, which act as middlemen between patients and insurers or employers, are aggressively moving into the market. One of the largest, Medco, has established a personalized-medicine group to recommend which genetic tests insurers should pay for. In February it acquired DNA Direct, a firm that specializes in analyzing genetic diagnostics, to aid in this effort. One of its largest competitors, CVS Caremark, increased its stake in a similar company, Generation Health, last December. Because such companies serve millions of people, they will play a critical role in making genetic tests broadly available and educating doctors about the benefits of offering such tests to their patients. *—Lauren Gravitz*

DATA SHOT

$400

The approximate cost of genetic testing to predict a patient's response to the commonly prescribed blood thinner warfarin.



A machine for DNA sequencing was invented by Leroy Hood and his colleagues at Caltech. In 1992, Hood and several others were granted U.S. patent 5,171,534 for an "Automated DNA Sequencing Technique." Replacing slow and expensive manual methods, this is one of the most important pieces of intellectual property in biotechnology; explore an interactive analysis by IPVision of the patent's impact on the innovation landscape at www.technologyreview.com/briefings/personalmed

MARKET TABLES

Companies to Watch

PUBLIC COMPANIES

Company	Revenues	Market cap	R&D expenses	
Roche www.roche.com	$47.9 billion	$146.8 billion	$8.7 billion	In 2007 it acquired 454 Life Sciences, which develops DNA sequencing machines, including a desktop sequencer suitable for rapid sequencing of small genomes or portions of a human genome; machines will be available sometime this year.
Affymetrix www.affymetrix.com	$316.9 million	$385.1 million	$84.5 million	A pioneer in commercializing DNA microarrays, which allow for large-scale analysis of genetic samples, the company has made acquisitions that will let it analyze proteins and other biomarkers.
Life Technologies lifetechnologies.com	$3.3 billion	$8.8 billion	$333.9 million	Created from the merger of Applied Biosystems and Invitrogen in 2008. Applied Biosystems' machines were instrumental in completing the Human Genome Project; it is now developing a range of next-generation sequencing instruments.
AstraZeneca astrazeneca.com	$32.1 billion	$68.1 billion	$5.2 billion	Has moved aggressively into personalized therapeutics; its drug olaparib is now being tested in cancer patients with specific genetic mutations.
Celera Genomics www.celera.com	$174.3 million	$545.7 million	$35.2 million	Is trying to broaden the reach of personalized medicine into cardiac health.
Celldex Therapeutics www.celldextherapeutics.com	$13.4 million	$139.1 million	$26.3 million	Is developing technology for protein analysis, which is critical for translating genetic data into therapeutically valuable knowledge.
GlaxoSmithKline www.gsk.com	$44.2 billion	$102.5 billion	$6.8 billion	Has worked with the FDA to develop tools for setting up clinical trials appropriate to personalized medicine.
Helicos Biosciences helicosbio.com	$2.9 million	$75.2 million	$24.6 million	Has set its sights on developing technology that can sequence a human genome in a day, at a cost of $1,000.
Amgen www.amgen.com	$14.6 billion	$57.8 billion	$2.3 billion	Its drug for colorectal cancer comes with a recommendation that patients be genetically screened to see if they would benefit from it.
Illumina illumina.com	$646.7 million	$4.6 billion	$100 million	Recently unveiled a machine that can sequence two genomes in a week for $10,000 each.

PRIVATE COMPANIES

Company	Founded	Funding amount	Investors	
23andMe www.23andme.com	2006	Not disclosed	Google, Genentech, New Enterprise Associates	Sells genetic testing directly to consumers; results include information about ancestry and about the subject's sensitivity to a range of drugs.
BioNanomatrix bionanomatrix.com	2003	$5.1 million	Battelle Ventures, Ben Franklin Technology Partners, KT Venture Group, 21Ventures	The nanochannel technology it's developing could be used to sequence single DNA molecules without reassembling many small sequences into a genome.
Complete Genomics www.completegenomics.com	2006	$91 million	Enterprise Partners, OVP Venture Partners, Prospect Venture Partners, Highland Capital Management, Genentech	Unlike other companies developing sequencing technology, it does not sell machines or reagents, instead offering bulk sequencing services to researchers.
Generation Health mygenerationhealth.com	2008	Not disclosed	CVS Caremark, Highland Capital Partners	Manages health benefits related to personalized medicine for insurance companies. As DNA testing becomes more common, this type of company will be increasingly important.
Integrated Diagnostics integrated-diagnostics.com	2009	$30 million	InterWest Partners, Wellcome Trust, Dievini Hopp BioTech Holding	Is developing diagnostic products based on genetic and protein analyses to look at tens to hundreds of disease markers simultaneously.
Knome knome.com	2007	Not disclosed	Privately funded	Will sequence and analyze the complete genome of any individual for $68,500.
Metabolon metabolon.com	2000	$30 million	Syngenta Ventures, Sevin Rosen Funds, Aurora Funds	Analyzes an array of metabolic markers to diagnose diseases or reactions to drugs.
Navigenics www.navigenics.com	2006	Over $40 million	Procter and Gamble, Kleiner Perkins Caufield and Byers, Mohr Davidow Ventures	Offers genetic testing directly to consumers and encourages doctors to incorporate testing into their practice.
Pacific Biosciences pacificbiosciences.com	2004	$266 million	Wellcome Trust, Mohr Davidow Ventures, Kleiner Perkins Caufield and Byers, Alloy Ventures	Is developing next-generation sequencing technology, with an approach that uses nanophotonics to analyze DNA.
Proventys proventys.com	2005	Not disclosed	Burrill and Company	Is developing software that will help doctors use genetic testing and clinical data to make prognoses and determine treatments.

MARKET TABLES

Research to Watch

Project	
Applied Statistical Genetics Group Wellcome Trust Sanger Institute www.sanger.ac.uk/research/projects/appliedstatisticalgenetics	Finding ways to analyze large amounts of genetic data and extract information related to diseases that involve multiple genes.
Cancer Biology and Genetics Program Sloan-Kettering Institute www.mskcc.org	Testing a microfluidic chip that will measure differences in how genes are expressed in tumors.
Coriell Personalized Medicine Collaborative Coriell Institute for Medical Research cpmc.coriell.org	Enrolling 100,000 participants in a research study to measure how genetic information can improve health.
Diagnostic Investigation of Sudden Cardiac Event Risk CardioDX www.cardiodx.com/clinical-studies/cardiac-arrhythmia	Developing a genetic test that will identify patients at risk of sudden cardiac death who should receive an implantable defibrillator.
EuroGenTest Catholic University of Leuven and others www.eurogentest.org	An EU-funded consortium seeking to standardize genetic testing and establish guidelines for doctors and patients.
Global Alliance for Pharmacogenomics National Institutes of Health, RIKEN Yokohama Institute www.nigms.nih.gov/Initiatives/PGRN/GAP	An American-Japanese scientific alliance studying pharmacogenomics across a broad array of medical conditions, including depression, AIDS, and asthma.
Pharmacogenomics Knowledge Base Stanford University Medical Center and others www.pharmgkb.org	An international consortium building a database detailing the influence of genetic variations on drug reactions.
Plavix, Effient Comparative Effectiveness Study Medco www.medcoresearch.com/community/pharmacogenomics	Investigating whether using genetic tests to determine a patient's sensitivity to certain drugs is more cost-effective than choosing drugs that are less affected by genetic variations.
The 1000 Genomes Project Wellcome Trust Sanger Institute, Beijing Genomics Institute Shenzen, National Human Genome Research Institute www.1000genomes.org	Sequencing the genomes of about 1,200 people around the world to create a database of biomedically relevant genetic variation.
The Cancer Genome Atlas National Cancer Institute, National Human Genome Research Institute cancergenome.nih.gov	Sequencing thousands of samples from over 20 types of tumors to understand the genetic changes that underlie these cancers.

REVIEWS

FINANCE

What's Wrong with Venture Capital?

THE OLD MECHANISM FOR FUNDING THE COMMERCIALIZATION OF NEW TECHNOLOGIES IS IN TROUBLE.

By JAMES SUROWIECKI

In the summer of 1996, Silicon Valley venture capitalists put a few million dollars into a telecom-equipment startup called Juniper Networks. Three years later, after a few more rounds of funding and the release of its first product, Juniper enjoyed an initial public offering of shares, or IPO. At the end of its first day of trading, it was worth nearly $5 billion, and within nine months, it was worth almost 10 times that. The original venture investors, meanwhile, were able to walk away with profits of better than 10,000 percent.

Around the same time Juniper went public, Silicon Valley venture capitalists were putting money into a new networking startup, Procket Networks. This time, the initial investments were bigger, and over successive rounds of financing, Procket collected almost $300 million in venture money. Three years after it started, though, the company had still not launched a product, and in 2004 its assets were acquired by Cisco in a fire-sale deal. This time the VCs walked away with just a fraction of their original investments.

The difference between those two stories is, of course, the difference between the world of the late-1990s technology-stock bubble and the world after that bubble burst. But of late, it also seems like the difference between the historical image of venture capital and the harsh reality of the current business. A decade ago, venture capitalists seemed like genuine alchemists, able to turn even startup dross into purest gold. In recent years, however, the industry has seemed less magical than mundane. Since 2004, its average five-year return has oscillated around zero. High-priced IPOs have become rare events, even as VCs have continued to pour tens of billions of dollars into new companies every year. As Fred Wilson, a principal at Union Square Ventures, bluntly puts it, "Venture capital funds, as a whole, basically made no money the entire decade."

BOULEVARD OF BROKEN DREAMS: WHY PUBLIC EFFORTS TO BOOST ENTREPRENEURSHIP AND VENTURE CAPITAL HAVE FAILED—AND WHAT TO DO ABOUT IT
Josh Lerner
Princeton University Press, 2009

Naturally, venture capitalists have not remained indifferent to these developments. On the contrary, the soul-searching has sometimes resembled Maoist self-criticism sessions. The word *crisis* has become ubiquitous. Matrix Capital founder Paul Ferri told the *Wall Street Journal* in 2006 that the industry does not now have "an economically viable business model." In the June 2005 issue of this magazine, Yankee Group founder Howard Anderson bid "good-bye to venture capital." And when the executive search firm Polachi and Co. asked a thousand VCs last summer "Is the venture capital business broken?" more than half said it was. When you consider the key role that venture capital has played in funding American innovation over the last 50 years, that conclusion seems ominous. *(For another practitioner's take on the state of venture capital, see Steve Jurvetson's Notebook "The Pace of Innovation Never Falters," p. 12.)*

Some of this breast-beating is, to be sure, inevitable. Booms and busts have been endemic to the venture capital industry since it was founded in the late 1950s. As Harvard's Josh Lerner puts it in *Boulevard of Broken Dreams,* his new book on the history of public efforts to boost venture capital, time and again "groups raised huge amounts of capital that they invested foolishly, either funding entrepreneurs who never should have raised capital in the first place, or else giving far too much money to promising entrepreneurs." *(See "Publicly Funding Entrepreneurship," Lerner's Notebook on the government's recent efforts to spur innovation, p. 12.)* And the busts that follow those frenzies tend to engender profound pessimism—in 1994, just before the boom of the late 1990s, Paul Gompers, then at the University of Chicago, published a major study of the industry titled "The Rise and Fall of Venture Capital." Given that we've just lived through the bursting of two asset bubbles, and that the stock market—the traditional exit for venture capitalists—has gone nowhere in 10 years, it would be surprising if people weren't gloomy.

THE EXCEPTION Google's successful initial public offering over five years ago did not usher in a new era of good times for venture capitalists; it merely served to underscore how rare these happy events have become.

Nonetheless, it would be a mistake to assume that the industry's problems will vanish once the economy picks up. Instead, it seems clear that at least some of the factors that have made huge returns rare are the result of structural—not cyclical—shifts, and that venture capitalists will need to adapt.

To begin with, the costs of starting companies and of making companies profitable in sectors like information technology have fallen dramatically thanks to open-source software, the globalization of engineering, the commodification of bandwidth and infrastructure, and other factors. Wilson, for instance, estimates that costs have fallen "at least an order of magnitude" in the past decade. That's given entrepreneurs more leverage, since they're less desperate for capital. At the same time, sectors where venture capital has traditionally made a huge impact, like IT and telecommunications, are no longer growing as fast as they once did. And much of the value that new businesses are creating in fields such as social networking is, at least for the moment, "nonmonetized"—the benefits that users get don't translate into dollars. There is now a generation on the Net whose governing assumption is that things should be free. Any assumption that they will be as lucrative a group of customers as corporate IT departments may be mistaken.

Finally, it's an open question whether IPOs will again become the gold mine they were for venture capitalists in the past. Just 13 venture-backed firms went public in 2009—down from 94 in 2004 and 271 at the height of the boom, in 1999. In an earlier era, Facebook and even Twitter would almost certainly have gone public. Yet neither company seems all that anxious to do so. The problem is on both sides: entrepreneurs don't yearn to take their companies public as they once did, and investors aren't clamoring for more public offerings. Running a public company is more difficult than ever: there are more rules to comply with, more pressure from shareholders, and, at least lately, more volatility. More important, IPO pricing is more rational than it once was. That is crucial, since turning startups into public companies has been the way venture capitalists made most of their money. Anderson, for one, thinks saner valuation is at the heart of the industry's problem. "The entire market has become more mature," he says. "This is not a bad thing in general, but it's not good for venture capitalists, because we love irrational markets. They make it much easier to have the outrageous winners you need in order to make the economics of the business work." Exceptions exist—battery maker A123 Systems (which Anderson invested in) raised $380 million when it went public last fall—but they have been rare.

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There are some signs of adaptation. Tim Draper of Draper Fisher Jurvetson (DFJ), for instance, argues that "the next eight to 10 years are going to be the greatest venture capital years in the history of the world." But he believes that the drivers of future innovation aren't in traditional locations: in addition to Silicon Valley, DFJ is investing in China, India, and Vietnam. Meanwhile, even if, as Paul Kedrosky of the Ewing Kauffman Foundation argues, "too many venture partnerships [are] continuing to invest in information technology because they always have," many VCs have begun funding companies in industries like media, education, and even finance, where technological change is creating disruptive innovations and, therefore, opportunities for profit.

But it won't be enough for VCs simply to change what they invest in and where they invest. The real problem is not complex: there's too much venture capital, and there are too many venture capitalists, for the industry to be really profitable. The industry as a whole now has about $200 billion under management, more than twice what it did in 1998, and venture funds invested $20 billion to $30 billion a year for most of the past decade. And on the level of individual funds, huge amounts of capital combined with falling startup costs have, in Anderson's words, made funds "muscle-bound": a $500 million fund can't make too many small investments, even if that's what would make economic sense, because the partners don't have the time to supervise hundreds of companies. (This is one reason, along with the desire to limit risk, that many VCs have started to wait until later rounds to invest.) In the absence of another bubble, there's no way for new companies to generate profits big enough to provide a reasonable return on $20 billion to $30 billion a year. Kedrosky, for one, argues that for the industry to consistently generate competitive returns, annual investment and money under management need to fall by more than half. And while Wilson describes himself as "very optimistic" about the com-

GETTY IMAGES

ing decade, he says that the industry "needs to return to the size and shape it was in the late '80s and early '90s."

The interesting thing is that this diagnosis is not especially controversial. Most people in the industry think there's too much money. It's like traffic, though: everyone thinks there's too much of that, but no one wants to take public transportation. And while in most businesses competition takes care of the problem by forcing the losers out, here winnowing takes much longer, because venture capital isn't like the stock market: if you get disillusioned, you can't just pull your money out of it. The limited partners who invest in venture capital funds make long-term, binding commitments to meet the "capital calls" of the general partners who manage the funds and make investments. This is, from the perspective of innovation, venture capital's great strength: instead of needing a quick return, it can afford to build companies. Nonetheless, it creates what Wilson calls "a huge amount of latency in the system." So even though the industry has been moving toward a more sensible balance between money under management and potential returns, it takes a long time to push underperformers out.

This suggests that the industry as a whole still has at least a few years of underperformance ahead. Although that's not good news for venture capital investors, it's not clear that it's a problem for the economy. What's peculiar about the debate over the brokenness of the venture capital model is that it isn't really a debate about whether it's important to have early-stage funding for innovative companies: everyone believes that. Nor is it an argument about whether venture capitalists add value: the complaints of many entrepreneurs notwithstanding, the historical evidence suggests that venture capital has played a key role in fostering innovation. In a study of Silicon Valley firms, for instance, academics Thomas Hellmann and Manju Puri found that venture-backed firms were significantly quicker than others to bring products to market and were more likely to pursue what they call an "innovator strategy." And in a study of patent data, Josh Lerner found that venture dollars were "three to four times as potent" as corporate R&D in encouraging innovation.

WHAT WE CARE ABOUT WHEN IT COMES TO VENTURE CAPITAL IS NOT WHETHER INVESTORS GET GOOD RETURNS OR VCS ARE WELL PAID. WE CARE ABOUT WHETHER NEW COMPANIES ARE GETTING STARTED AND INNOVATIONS ARE BEING FUNDED.

If venture capital is both necessary and useful, then, why does it matter, from a societal point of view, if it's oversupplied? What we care about, after all, is not whether investors get good returns or VCs are well paid. We care about whether new companies are getting started and innovations are being funded. One of the fundamental truths of profitable innovation is that it is hard, if not impossible, to identify in advance. (That's why the familiar venture capital model depends on having a couple of huge hits in a portfolio to outweigh all the mediocre results and outright misses.) So while the shakeout will be welcome, it may actually be more important for the well-being of the industry than for the rest of us. As Tim Draper says, "There are never enough VCs or entrepreneurs or money for new efforts." After all, even though venture investors undoubtedly put too much money into me-too software companies and cleantech firms that never panned out, would we really have preferred that money to have gone into some bank's collateralized debt obligation instead?

Probably, no. But there are reasons to think that a too-flush venture capital industry isn't a good thing. First of all, since VCs get a percentage of assets under management, having tens of billions come into the industry every year makes it possible for a venture capitalist to make a good living even from investments that go nowhere. That's not a recipe for creating focused VCs. And the "muscle-bound" problem is real, too: to the extent that having too much money means venture capitalists wait to enter until later rounds of financing, the value that they add is reduced. It's also likely that because the size of these funds has required VCs to spread their investments across more companies, their effectiveness as monitors of corporate performance has been diminished. To many entrepreneurs, this may not sound so bad, but Lerner's research, at least, suggests that the guidance and monitoring VCs provide is an important part of why VC-backed firms have historically done better at sparking innovation. It may be a coincidence that the oversupply of venture capital has coincided with an era that produced, arguably, just two transformative venture-funded startups: Facebook and Twitter *(for an analysis of Twitter's business, see "Can Twitter Make Money?" p. 52)*. But it may also be that the industry as a whole just got a little too comfortable.

That's changing, for the good: VC funding was just $17.7 billion last year, down 40 percent from the year before. And although it will be painful, the industry needs investors to leave if it's going to return to a more rational size. It is highly unlikely that the pendulum will swing back too far—that venture capital will become underfunded. The allure of huge profits is not going to vanish. And the activities of venture capitalists are still associated more with hugely profitable investments like Juniper (and, before it, Cisco, Apple, and Digital Equipment Corporation) than with ventures like Procket.

Venture capitalists, like entrepreneurs, are overconfident: they believe they can identify and exploit profit opportunities that others are missing. If this may not be a great thing for them or their investors, it's a good thing for the rest of us, since it guarantees a constant flow of new money into new businesses. Venture capital needs to become a more rational business. But not *too* rational. TR

JAMES SUROWIECKI WRITES "THE FINANCIAL PAGE" FOR THE *NEW YORKER*.

MARK OSTOW

CHEMISTRY

A Rose by Another Name

A FOOD CRITIC EXPLORES THE SYNTHESIS OF THE SCENTS IN MODERN FRAGRANCES.

By CORBY KUMMER

For most of my adult life, I've been fragrance-free. That's not because I don't like scents, perfumes, eaux de cologne, and the like. I do. But I outgrew the scents I used as a teenager—Eau Sauvage and, yes, Canoe. I stopped dousing myself. Or perhaps I moved my powers of appreciation to my palate. I'm a food writer, and I try to identify and remember everything I eat.

Because I'm a food writer, I know how much industrial food depends on odorants, as molecules created for fragrance or flavors are called. And I'm interested in how the new "hypercuisine" or "molecular gastronomy" draws upon the technologies of industrial food to create new flavors: see the profile I wrote of Grant Achatz, the chef at Alinea in Chicago *("The Alchemist," January/February 2007 and at technologyreview.com)*. But the food and fragrance industries use odorants in very different ways.

Food manufacturers buy odorants that mimic real flavors, although they goose them until they are almost unrecognizable—take truffle oil, which tastes nothing like truffles. But fragrance manufacturers mostly don't bother to imitate nature. Perfumes are a mixture of natural essences, which are expensive because they require so many flowers, herbs, or spices (the extraction rate of flowers in an essential oil is at best 1 percent, and often closer to 0.1 percent), and synthetic odorants. The synthetics include "effect aroma chemicals" with little smell of their own, which extend and enhance other molecules, and "character impact chemicals," which either cheaply mimic natural ingredients or do something that hypercuisine chefs envy: smell like nothing in nature. Blended, these ingredients can make a perfume modern, fresh, sexy, and fascinating. Or blaringly, nauseatingly domineering.

EAU SAUVAGE
Christian Dior
Created 1966 by Edmond Roudnitska. 3.4 ounces eau de toilette, $72.

EAU DE GUERLAIN
Guerlain
Created 1974 by Jean-Paul Guerlain. 3.4 ounces eau de toilette, $96.

BIGARADE CONCENTRÉE
Editions de Parfums Frédéric Malle
Created 2002 by Jean-Claude Ellena. 3.4 ounces perfume, $210.

I like new things. I was curious whether a new perfume, particularly one made with novel scents, could appeal to me.

WE SMELL

Finding your own fragrance can be as difficult and complicated as finding the right partner in life, and a lot harder than deciding what to eat. It's sexual in its overtones, which helps explain why $38 billion worth of perfume is sold every year. Cruising the first floor of Saks Fifth Avenue in Boston is like cruising a certain kind of bar: you get to test anything that appeals, brutally snub whatever bores or repels you, and take home whatever you find really attractive.

In perfume aisles Luca Turin is an *homme aux femmes*, ready to be ravished. Turin is a biophysicist, currently at MIT, who has a celebrated, notorious passion for perfume. He didn't invent the discipline of perfume criticism, but he redefined it, opening up a new branch of aesthetic evaluation with a dazzling field of reference and punchy pungency. The English magazine *Prospect* called his 2008 book *Perfumes: The Guide*, which he wrote with Tania Sanchez, "bigoted, snarling, monomaniacal, subjective, triumphalist, and quite magnificent." He and Sanchez are Pauline Kaels of the fragrance world, revered and reviled.

The two (who are married) are sensual in their reviews. Turin, who met me at Saks, told me that the 1971 Chanel No. 19 was a "bitch perfume, like green sharkskin pumps." He writes of a perfume by Le Labo that after three minutes, "Oud 27 becomes properly pornographic: a wet-hair note and a couple of macrocyclic musks of the kind found near the rear end of deer take over … . Great fun, brilliant perfumery, and, for once, really raunchy."

Any lesson in the art and history of perfumery starts at the Chanel counter, to which Turin kept returning during our pinballing tour. That's because Chanel No. 5 is the

definitively modern, composed perfume—a pretty, very sweet floral made with jasmine and rose, which are always expensive, and a surprising amount of violet, which is to the fragrance industry what vanilla is to food: the first successfully synthesized floral. But Chanel No. 5 also has a significant proportion of novel chemicals: a blend of aliphatic aldehydes that both buffer the sweetness and enhance it, giving the perfume an artificial

ARTIST, SCIENTIST Luca Turin is an MIT biophysicist, a fragrance chemist, and the coauthor of *Perfumes: The Guide*.

scent. They also give it structure. The Belgian perfumer René Laruelle calls synthetics the bones of fragrance, naturals the flesh.

Turin spent the most time with me at the counters of Chanel, Guerlain, and Estée Lauder, the last of which he said was underappreciated. He wanted to smell a new Lauder perfume: Jasmine White Moss. It is a classic *chypre*, the French word for "cypress" and the name of a famous 1917 perfume that blended sweet amber resin, citrus, and woody, oak-moss notes in what became an endlessly varied triad. The current classic of the genre is Chanel's Cristalle. Turin pronounced the new Lauder "as good as it gets." I smelled both Cristalle and Jasmine White Moss at length—the "heart" and the "drydown," after 15 minutes to an hour, are what really matters—and found Cristalle to be admirably formal and cold, as Turin said I would. By contrast, Jasmine White Moss was startlingly sweet at first but was then reined in by the sterner oak moss and wood.

Turin likes *chypres*, but he's fascinated by the "wonderfully spare aesthetic" of what he calls *nouvelle parfumerie*, which is characterized by dry wood, smoke, tar, and the abundant use of aromas that don't exist in nature. Landmarks include Bertrand Duchaufour's 2004 Timbuktu for L'Artisan Parfumeur and Comme des Garçons' 2 Woman, "rasping and caressing," designed in 1999 by Duchaufour's colleague Mark Buxton. At Saks, Turin gave me a whiff of another fragrance he guesses is 80 percent synthetic—the same proportion he estimates in the Lauder, but this one designed to be new and strange: Rush, by Gucci. He loves it. "This creature may be from outer space," says *The Guide*, "but its blood is warm." I found it like a neon sign as bloody red as its box—impossibly strange, and frankly emetic.

IT'S CHEMISTRY

How do chemists find these chemicals that mimic natural fragrances, enhance aromas, or smell completely new? By trial and error. Fragrance chemists can build the molecules that produce a smell, and then test variants. But they have never been able to design odorants without weeks or months of labor and expensive trials. Turin says he has found a way to do just that, guided by a different theory of how molecules stimulate smell perception. It is not his reviews, however brilliant, but *The Secret of Scent* (2006), describing the molecular-vibration theory of olfaction, that he hopes will be his legacy.

For decades the guiding theory was that a molecule's shape determined smell: in lock-and-key fashion, a molecule would bind to a receptor site in the nose, ultimately sending signals to the brain that result in the experience of a smell. The lock-and-key model had proved widely applicable in biochemistry, and it seemed natural to extend it to olfaction, as Linus Pauling did in 1946. But 50 years of fragrance chemistry has shown little correlation between molecular shape and odor. Musks, for example, have very similar shapes and very different odors; tiny changes to the molecule of, say, an elusive floral fragrance can wreck its smell. Turin revived a theory, originated in the 1920s, that posited a correlation between molecular vibrations and smells. The English chemist Malcolm Dyson formally proposed it in 1938, and Robert H. Wright, a Canadian chemist and physicist, advanced it in a 1977 paper. But they both lacked an explanatory mechanism.

Any mechanism would have to explain how the nose can do the work of a spectrometer, without infrared beams to excite vibration. Since humans have only 347 smell receptors, a discovery announced in 1991 by Linda Buck and Richard Axel, each receptor must somehow recognize thousands of smells. In Turin's theory, an odorant molecule that fits into a receptor's binding site can switch on the receptor only if the molecule has a particular vibration, a quantum of energy matching the difference between two energy levels in the receptor. Once the sluiceway is open, electrons can travel through the molecule across the receptor, which recognizes the smell in much the way that cone cells in the retina recognize color by frequencies, or hair cells in the cochlea recognize sound vibrations.

Turin published his electron-tunneling mechanism in 1996 in *Chemical Senses*. Some parts of the theory were, and remain, unproved. Isotopes, for example, are identical in shape but should smell different from one another because their slightly different weights should produce slightly different vibrations. Turin reported that they did. But his finding proved hard to reproduce in studies involving naïve subjects: differences in smell are subtle, and perception varies from subject to subject. The fail-

MARK OSTOW

ure to confirm odor differences between isotopes, which seemed to disprove the theory, was reported in a paper in a 2004 issue of *Nature Neuroscience*, accompanied by a harsh editorial. But recent studies are turning the tide Turin's way. A 2007 paper in *Physical Review Letters* showed that his mechanism was physically plausible; and Greek researchers are preparing to publish a paper showing that fruit flies can, in fact, smell the difference between isotopes. (In 2003, Turin's trials in forwarding his theory were the subject of *The Emperor of Scent* by Chandler Burr, who now writes about perfume for the *New York Times*.)

While his theory was under attack, Turin consoled himself, as Noël Coward would say, with the bitter palliative of commercial success. From 2000 to 2007 he was chief scientist for Flexitral, whose main business was creating replacements for 26 fragrances that the European Union had restricted or banned as possible allergens. He was using vibrational theory to design molecules every day "and getting a tremendously high success rate," he says. "I could calculate whether a smell would be right or not."

All very practical, and potentially very profitable—but not madly artistic. "One would like to invent new smells, but business is business," Turin says. Yet at the company he did achieve what he calls a long-held dream: a "drop-dead lily of the valley." *Muguet*, the lovely French word for the flower, is the mountain any fragrance chemist hopes to scale. There has been no truly accurate rendition of its all-white scent, which combines soapy rose and cut grass. Edmond Roudnitska's Diorissimo, created in 1956, came the closest; it established Roudnitska, Turin writes, as the "Mozart of postwar French perfumery." Two of the chemicals Roudnitska discovered to be key components were later identified as potential allergens, and their use has been restricted. On a mountain on a skiing holiday, Turin got the idea for a molecule he guessed would smell right. That night he faxed a sketch of it to chemists at his lab and asked if they could make it. Two days later, they reported that the whole laboratory smelled of lily of the valley. It was "an epiphany," Turin says. "Like a Roman emperor, I can die now."

Instead, he left the business for what he calls a "science break": at MIT he is working on an artificial nose.

A MATTER OF TASTE

Could I outgrow Eau Sauvage and embrace the new? In a long smelling session at the New York offices of Robertet, an international fragrance firm, I discovered one reason I used Eau Sauvage in the first place: it contains a novel synthetic, and one I *like*. To historians of fragrance, Eau Sauvage is famous because it was the first perfume to use hedione, an "effect aroma" that, Turin says, "lubricates" a fragrance, as if one were licking one's lips. Discovered in 1961 and put to use by Roudnitska five years later, hedione gives Eau Sauvage what Turin describes as a "strange, glittering freshness." The fragrance could cut through a 1960s smoke-filled room (cigarette smoke has become the great missing ingredient in older perfumes) with its mixture of citrus, pine, and rosemary.

Jérôme Epinette, the proper, precise fragrance chemist at Robertet, let me smell hedione in his shiny, glass-walled, glass-bottle-lined lab on Fifth Avenue. Robertet designs fragrances for many U.S. designers and brands, and it is Epinette who translates vague ideas into samples sent off for evaluation and, if approved, production. I loved hedione, not because it reminded me of Eau Sauvage but because it smells a little like concentrated peony petals after a spring rain. Indeed, Epinette told me that he describes it to clients as "petal-ly" and "transparent."

"Transparent," "fresh": these are the qualities that became popular after the complex, big fragrances of the 1980s, and they can be found in many fruity, food-y fragrances, as Paul Austin, an Australian-born fragrance consultant who was a longtime top executive for Quest International, the large fragrance firm since bought out by rival Givaudan, told me. Unchallenging, foodlike fragrances

now appeal to more sophisticated European noses, too, he said, though Europeans once preferred the "intellectual" *chypre* genre.

And yet ... Eau Sauvage, *dépassé* as it may be, is still admired for its structure, and Austin says it had more character than many of the mainstream scents "we in the industry produce today." In his guide Turin writes, "I always forget how good this darned thing is. Part of the reason I don't wear it is that it reminds me of my youth." He embraces the new!

Then, in our madcap Saks round, Turin randomly sprayed on a Guerlain eau de toilette that, he said, was the only thing he wore for years. I loved it. Eau de Guerlain is pure, unsweet citrus, with a lingering light verbena scent on the drydown. "If you want citrus, there is simply nothing better out there," his review says. Bergamot and citrus, also the dominant notes in Eau Sauvage, are apparently what I want. It makes sense. Verbena was the scent of my childhood: my mother ordered boxes of specially milled lemon verbena soap for every bathroom.

Eau de Guerlain it is, then. Well ... there was *one* new perfume that I kept returning to with an almost physical craving, even after smelling dozens: Bigarade Concentrée, sold by Malle and created by Jean-Claude Ellena, now the house fragrance designer for Hermès, where he designed Eau de Pamplemousse Rose, another citrus I liked. Bigarade Concentrée smells powerfully of bitter Seville oranges, with nothing sweet or false about it; Turin likes the "interesting mixture of citrus friendliness and resinous austerity." But I wouldn't pay the $210 for the 3.4-ounce bottle (the same size bottle of Eau de Guerlain costs less than $100).

Maybe my simple taste marks me as a cook. "All chefs like citrus," Lev Glazman, who creates bespoke scents as head of fragrances for the Boston-based firm Fresh, told me. "It doesn't interfere with what they're cooking." So sue me. My search for the new resumes—with flavors. TR

CORBY KUMMER IS A SENIOR EDITOR AT THE *ATLANTIC*, WHERE HE WRITES ABOUT FOOD.

AVIATION

Reinventing the Commercial Jet

THE LONG-DELAYED BOEING 787 IS A LESSON IN THE LIMITS OF OUTSOURCING. IT IS ALSO A PREVIEW OF THE FUTURE OF AIR TRAVEL.

By DAVID TALBOT

Nearly seven years ago, when I visited Boeing's cavernous manufacturing site in Everett, WA, the sight of machinists playing ping-pong in a vast but idle shop seemed to symbolize the stagnant state of the aviation industry. Air travel had not recovered from the terrorist attacks of September 11, 2001. And Boeing was facing stiff competition: Airbus, its European rival, had made innovative advances in commercial jets, such as rear tail pieces made from lightweight composites. Worse, Airbus was gearing up to build the A380 superjumbo jet—a higher-capacity, more efficient competitor to Boeing's iconic 747.

BOEING 787 DREAMLINER

Boeing needed to do something bold. So it bet its business on a medium-sized advanced aircraft called the 7E7—today known as the 787 Dreamliner—that would be 20 percent more fuel-efficient than other jets of comparable size and cost less to maintain. Such a jet would make direct flights between far-flung smaller cities (say, Boston and Bangalore) cost-effective. "It's the future. It really is," Mark Jenks, a Boeing vice president who was then director of technology integration for the 7E7 program, said to me in 2003. "If we get it wrong, it's the end. And everyone here knows that."

Boeing's plane would greatly increase the use of advanced composites—layers of carbon fibers embedded in epoxy resin to form durable, lightweight materials. The 787 structure would be 50 percent composite, compared with just 12 percent in Boeing's previous jet, the 777, and 23 percent in the Airbus A380. For the first time in commercial aviation, the entire tube of the fuselage would be a single piece of composite, replacing the customary aluminum alloy skin affixed to aluminum alloy ribs. In another first, the wings and the center wing box—a chunk of fuselage to which the wing structures attach—would also be made of composites.

Innovation extended to the design and manufacturing process. Airbus and Boeing had long subcontracted some manufacturing, and Airbus had even invited some subcontractors to invest and share the risk in the A380. But in an effort to reduce its own investment and cut costs, "Boeing took it a lot further," says Hans Weber, owner of San Diego–based TECOP International, a technical consultant to the aviation industry and government agencies including the Federal Aviation Administration. Airbus had never outsourced design or the manufacture of the main airframe. With the 787, Boeing did both.

On paper, customers were impressed; by the end of 2007, the 787 was the hottest-selling jet in history. But when the first one took wing for its first test flight in December, it was the most delayed commercial jet in the firm's history—28 months behind schedule. The 787 had become bogged down in a saga of parts shortages, subcontractor failures, and weaknesses in crucial composite structures, requiring retrofits and redesigns.

WHERE'S THE DUCT TAPE?

So what went wrong? For starters, the company lost track of certain details—namely, fasteners. Building a single Boeing 777 requires 2.7 million titanium, aluminum, and stainless-steel bolts, rivets, and other fasteners peculiar to airframe manufacture.

WWW See more images of the Boeing 787: **www.technologyreview.com/boeing787**

MATERIALS SCIENCE? A Boeing 787 Dreamliner undergoes final assembly in Everett, WA. The jet's fuselage and wings are made entirely of composite materials, a first in commercial aviation.

ED TURNER/BOEING

And the 787 would need more fasteners made of the titanium alloys that are least susceptible to corrosion when in contact with carbon composites.

As the 787 project geared up, the industry was already in the midst of a fastener shortage. But Boeing's extensive outsourcing strategy compounded this problem. The back of the fuselage was made by Vought Aircraft Industries in South Carolina; a middle chunk by Alenia Aeronautica in Italy; the nose by Spirit AeroSystems in Kansas. In Japan, Mitsubishi, Fuji, and Kawasaki Heavy Industries built the wing structures—and Kawasaki built yet another piece of fuselage.

Suppliers were ordering fasteners in different ways and on different schedules; as a result, the fastener manufacturers found it difficult to make coherent production plans, according to a recent case study by the University of Michigan's Ross School of Business that drew on Boeing reports and interviews with company employees. This bogged down manufacturing. "Boeing was caught off guard," says Ravi Anupindi, a professor of operations management at Ross. "By the time they knew about it, it was at a crisis stage." To solve the problem, the company wound up taking over the ordering of all fasteners.

Next, problems arose with the composite structures. In March 2008, Boeing said that parts of the center wing box, built by Fuji Heavy Industries, had unexpectedly buckled during stress testing. This caused a six-month setback as Boeing added aluminum reinforcements to the boxes and changed the designs of future ones. Then, days before a planned first flight in June 2009, the company discovered that composite "stringers" joining the main wing structure to the center wing box—the most severely stressed connections on any plane—had delaminated in testing. Boeing had to remake the wing-body connections, adding, among other things, 34 new titanium fittings.

The full story behind these issues has not been revealed, and Boeing provided no interviews for this story. "It's hard to tell where a lack of oversight by Boeing ends and a bad contractor performance begins," says Richard Aboulafia, vice president of the Teal Group, a think tank and consultant to the civil and military aviation industries. "Getting other people to build things for them worked well for Boeing, decade after decade. So with the 787, it was just faith. It might have worked with traditional designs, but with composites and new techniques, it was guaranteed to be a disaster."

TOULOUSE GOOSE

The problems and delays contributed to the $3.5 billion in charges the company took last year. And Boeing found it necessary to buy the South Carolina plant of Vought, which had fallen behind on its fuselage work, and to build a second fuselage assembly line. The company recognized belatedly that its outsourcing had gone too far, says Morris Cohen, a professor of manufacturing and logistics at the Wharton School at the University of Pennsylvania. "We see more and more outsourcing of manufacturing, globally, in high-tech industries," Cohen says. "We are discovering that as you move down that path, the challenges are not trivial. I don't think companies have paid enough attention to how to manage supply chains from a strategic perspective."

The clearest consequence, besides the costly delays, is that the first few 787s will probably be heavier than the targeted 108 tons. Nevertheless, the first 787s are scheduled to be delivered this year. And as long as the plane ultimately performs as advertised, the delays may not harm Boeing's long-term reputation. "Boeing can very easily redeem itself by producing a product that the market wants," says Aboulafia. Airlines and passengers, he adds, "remember the product, not how it was executed."

Meanwhile, the Airbus A380 program has faced its own manufacturing glitches. More significant, the plane has found relatively few buyers; with a capacity between 525 and 853 passengers, it is simply too big to make sense for many airlines. Whereas Boeing has logged more than 800 orders for the 787, only about 200 have come in for the A380, earning the aircraft—whose maker is headquartered in Toulouse, France—the nickname "Toulouse Goose," after Howard Hughes's infamous "Spruce Goose," the wood-framed World War II–era behemoth that never made it beyond a single prototype.

Even if the 787 passes through all the turbulence, Boeing can't rest for long. Airbus now has a 787 competitor waiting in the wings: the midsize A350, also 50 percent composite. About 500 orders have come in, and Airbus says it's on track to start delivering the aircraft in 2013. So in a sense, the 787 program seems likely to pay off one way or another. If it provided a hard lesson about the limits of outsourcing and the risks of innovating with composite materials, the bold design also gave Boeing a much-needed head start on the next phase of innovation in commercial aviation. TR

DAVID TALBOT IS *TECHNOLOGY REVIEW*'S CHIEF CORRESPONDENT.

B BAR CODE

To help keep track of samples, a bar code is printed on the test cartridge and the underlying slide.

A DISPOSABLE CARTRIDGE

A single-use cartridge uses a combination of chemical reactions to isolate fragments of DNA from a patient sample and test them for specific genetic characteristics. The top half of the cartridge is discarded after this process is complete, leaving a prepared glass slide behind.

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Personalized Medicine on the Spot

A NEW DEVICE CAN RAPIDLY TEST BIOLOGICAL SAMPLES FOR GENETIC VARIATIONS THAT COULD CAUSE DANGEROUS REACTIONS TO SOME DRUGS.

BY ERICA NAONE

DIFFERENT PEOPLE CAN react to drugs in different ways, and in some cases the response can be predicted from their genes. For example, the drug warfarin, often used to prevent blood clots, can cause dangerous bleeding in some patients. Researchers have identified two genetic variations that can increase this risk.

Tests for this type of individual genetic variation have been available for a long time, but in many cases they cost too much and take too long. Nanosphere, a startup out of Northwestern University that's based in Northbrook, IL, hopes to change that. Its Verigene system, which takes just a few hours to analyze DNA from blood or other material, allows doctors to test for genetic variations without having to send samples out to a lab.

C REAGENT WELLS

The necessary ingredients for the chemical reactions used to process the DNA are stored in wells located around the edges of the test cartridge. After the DNA is extracted from a sample, the machine uses air pressure and mechanical valves to release the ingredients from the wells as needed. Strands of DNA that are complementary to the target sequences are used to bind those sequences to the glass slide below the cartridge, as well as to gold nanoparticles that will allow the DNA to be detected when exposed to light. The cartridge washes away any excess DNA or nanoparticles and then sets off a reaction that coats the remaining nanoparticles with silver, which makes it easier to scan for them.

CHRISTOPHER HARTING

D DNA LOADING CHAMBER

A DNA sample is loaded into the port shown here. Sonic energy, applied when the cartridge is inserted into the machine that processes the samples, breaks the DNA into small fragments and separates it into its two complementary strands so that it can be captured on the surface of the glass slide.

E GLASS SLIDE (MICROARRAY)

After the chemical reactions have finished, the target DNA remains on the surface of the prepared glass slide, tagged by silver-coated gold nanoparticles. The Verigene's reader can read the slide by shining light into it and measuring how that light is scattered by the tagged DNA. The system can be used to look for single or multiple genetic targets.

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Scaling Up Solar Power

APPLIED MATERIALS MAKES THE EQUIPMENT NEEDED TO PRODUCE THE BIGGEST SOLAR PANELS IN THE WORLD.

By KATHERINE BOURZAC

In 2006, semiconductor-equipment giant Applied Materials got into the solar-power market in a big way. At the company's headquarters in Santa Clara, CA, you can see just how big: a ceiling-mounted crane lifts a piece of glass the size of a garage door onto a table for testing. The glass sheet, covered with a thin orange film of amorphous silicon, is destined to become one of the world's largest solar panels.

Applied Materials developed the equipment to produce these extremely large photovoltaic panels in order to lower the price of solar power—crucial if solar is to compete on price with fossil-fuel electricity. The value of a solar installation comes down to the cost of each watt of power it can produce over the lifetime of a panel, and Applied Materials' panels bring down costs in two ways. The equipment for manufacturing thin-film solar cells operates more efficiently when the panels are bigger. And larger modules need less hardware and labor to wire them together and support them.

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Applied Materials, which was already the largest equipment supplier to the semiconductor and liquid-crystal-display industries, brought its expertise to solar power in 2006. The company's photovoltaics and its display backplanes are both based on glass panels coated with amorphous silicon. Its production facilities were already set up to make those panels in 10 sizes, so achieving the best cost per watt was simply a matter of picking the right surface area, says Jim Cushing, senior director of the photovoltaic-equipment line. The result was "by far the fastest ramp to production in the PV industry," he says—from lab to market in just under two years.

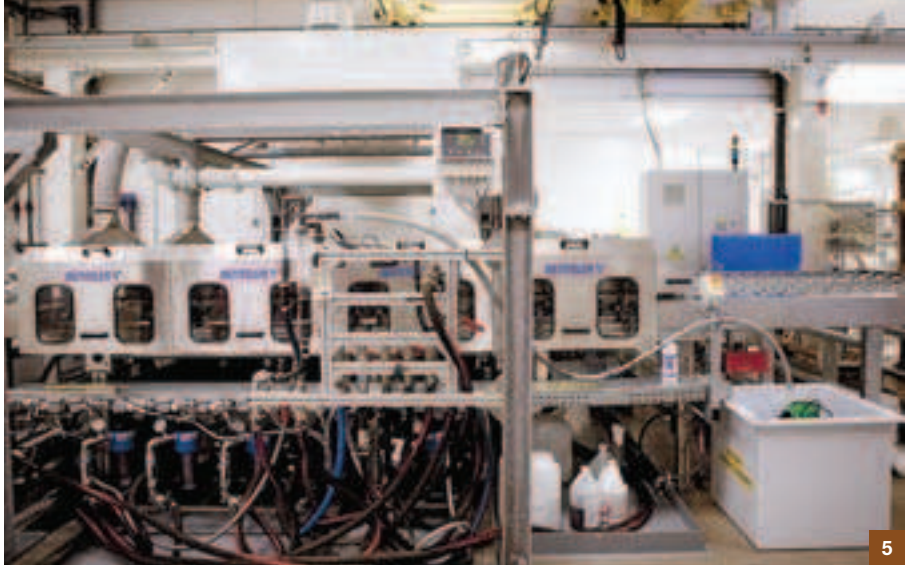
JEN SISKA

1. Technicians at Applied Materials test a laser scribe machine, part of the company's equipment line for making the world's largest solar panels. The lasers etch the outlines of solar cells into a transparent conductive oxide that coats a glass panel.
2. The panel travels down a conveyor belt toward a robotic loading arm, visible in front of a technician.
3. Glass panels are loaded into the racks of a two-story vapor deposition chamber, where they are coated with a thin film of amorphous silicon.
4. A worker uses a ceiling-mounted crane to move a panel coated with orange amorphous silicon.

Applied Materials now sells a complete set of equipment for transforming large glass panels into thin-film solar cells, transporting it to manufacturers in several shipping containers. The company claims that each factory using its equipment can produce enough solar cells every year to generate 80 megawatts of power, enough to provide energy for 35,000 U.S. homes during peak hours of electricity use.

The process of building the solar panels themselves starts with glass sheets 2.2 by 2.6 meters in area and only 3.2 millimeters thick. These come to a factory precoated with a micrometer-thick film of a transparent conductive metal oxide that will serve as the top electrical contact in the finished panel. A robotic arm shaped like the business end of a forklift loads the delicate glass sheet onto the metal rollers of a conveyor belt, which moves it through a cleaner and then through a seamer that reinforces its edges to prevent chipping during manufacturing. The panel then travels through a machine called a laser scribe, which carves lines through the conductive coating to define the boundaries of each of 216 cells on the panel.

The panel is now ready to be coated with two silicon films that will absorb sunlight and convert its energy into electrical current. First is a layer of amorphous silicon, which strongly absorbs light from the blue end of the spectrum. A second robotic arm slides the panel into the airlock of an apparatus called a plasma-enhanced chemical-vapor deposition chamber. Inside, the air is pumped out; silane, a gas composed of silicon and hydrogen, is pumped in and ionized. In the result-



5. The panels are washed in machines like this one at several points in the manufacturing process, first to remove the protective powder used to prevent scratching during shipping and then to remove any debris left behind after each of the etching steps.
6. Completed solar panels are installed at a testing facility at Applied Materials' headquarters in Santa Clara, CA, where their performance is monitored over time and under different weather conditions.

ing reaction, the gas decomposes, depositing the silicon uniformly on the glass.

Conveyer belts and robots then move each panel down the line to one of three additional vapor deposition chambers, where it is coated with a film of multicrystalline silicon. This layer absorbs red light, allowing the panels to take advantage of more of the energy in sunlight. Forming multicrystalline silicon takes time and care, but having three systems perform this step on different panels in parallel keeps it from slowing down the entire manufacturing process.

Moving down the conveyer belt, each panel goes through another laser scribe to carve the silicon films into cells whose boundaries align with the patterns in the conductive layer. The panels are then coated with three layers of metal that act as a back electrical contact; after another scribing step to shape a contact for each cell, they are nearly finished. If the manufacturer wants to cut the giant panels in half or even into four pieces, that happens at this point. Then, to ensure that a person who touches the edges of the finished panel won't get electrocuted, the borders of the conductive areas are edged off and the glass is reseamed to fill in the space.

Next, a top piece of glass is laminated to each panel in a process similar to that used in making car windshields. Finally, a junction box for carrying electricity from the panel is added to the back. Each completed panel is exposed to a solar simulator to test its output and then marked with a performance rating.

When Applied Materials started producing equipment for making the large modules, many in the business assumed that each panel would be sliced into smaller pieces, says John Benner, manager of PV-industry partnerships at the National Renewable Energy Laboratory in Golden, CO. But the company made a good case for leaving them intact. Because of their large area, the modules have among the highest power outputs in the industry—about 500 watts. The large size leads to savings on installation costs that help the panels compete with other thin-film systems on the market. The cost of electricity generated by the giant panels is $3.50 a watt, including installation.

Panels of this size are best suited for use in massive ground-based solar farms. Several such facilities have already been built, including a 500-kilowatt farm in Neustadt, Germany, that contains thousands of modules. Seven factories equipped with the technology are up and running at full volume and have manufactured more than a million of the modules.

The next challenge Applied Materials has set itself is to bring manufacturing costs down to $1 per watt by the end of this year. Its thin-film modules will have to compete with those made by other companies that are exploring alternatives to silicon—alternatives that are expected to reduce manufacturing and materials costs even further. TR

www Watch giant solar cells being made: **technologyreview.com/demo**

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About Your Professor

Dr. Scott E. Page is Collegiate Professor of Political Science, Complex Systems, and Economics at the University of Michigan. He received his Ph.D. in Managerial Economics and Decision Sciences from Northwestern University. An external faculty member of the Santa Fe Institute, Professor Page is the coauthor of *Complex Adaptive Systems: An Introduction to Computational Models of Social Life*.

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FROM THE LABS

BIOMEDICINE

An Anti-Cancer Implant

A POLYMER DISC TRIGGERS AN IMMUNE ATTACK TO SHRINK TUMORS

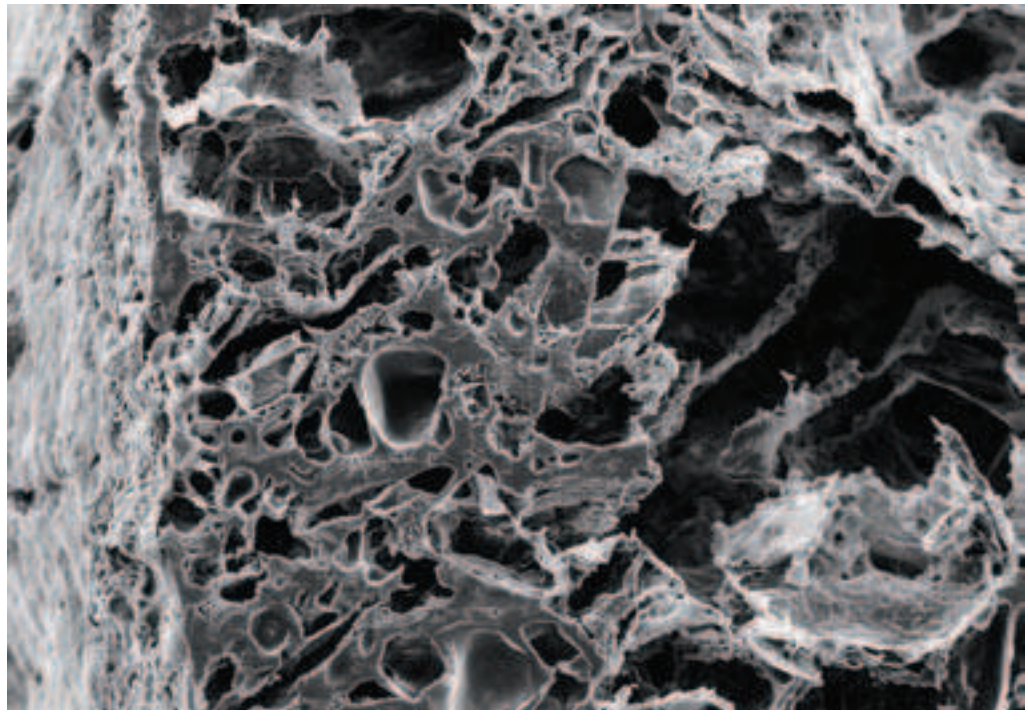
SOURCE: "IN SITU REGULATION OF DC SUBSETS AND T CELLS MEDIATES TUMOR REGRESSION IN MICE"
David J. Mooney et al.
Science Translational Medicine 1(8): 8ra19

Results: An implantable disc acts as a therapeutic vaccine against cancer, triggering the immune system to attack malignant cells. It slowed cancer growth and increased survival time in mice with melanoma tumors. The cancers completely disappeared in 20 to 50 percent of animals given two vaccinations; the success rate depended on how long the tumors had been growing.

Why it matters: This is the first vaccine to shrink tumors in rodents, rather than just slowing their growth. (A number of other therapeutic cancer vaccines are under development, but none has been approved by the U.S. Food and Drug Administration.) The vaccine appears to suppress a part of the immune system that typically neutralizes an immune response after it's achieved its initial goal. The ability to do this might be important in stopping tumors from recurring.

Methods: Researchers impregnated a polymer scaffold with three ingredients. Cytokines, signaling molecules produced by the immune system, attract immune cells known as dendritic cells into the implant. Fragments of genetic material designed to mimic bacterial DNA alert those immune cells that a foreign invader is present. The implant also contains ground-up pieces of the patient's tumor, which show the dendritic cells what to attack. The dendritic cells take up the tumor molecules as they move through the scaffold; then they travel to the lymph nodes, where they present the molecules to a different set of immune cells, triggering them to attack.

Next steps: Researchers will examine whether the same strategy can shrink other types of tumors. A startup called InCytu, based in Lincoln, RI, is developing the technology for human testing.



CANCER KILLER A cross-section of a polymer matrix designed to prime the immune system against cancer.

IMAGE COURTESY OF EDWARD DOHERTY, OMAR ALI, AND MICROVISION LABS.

Synthetic Platelets

NANOPARTICLES STIMULATE BLOOD CLOTS

SOURCE: "INTRAVENOUS HEMOSTAT: NANOTECHNOLOGY TO HALT BLEEDING"
Erin B. Lavik et al.
Science Translational Medicine 1(11): 11ra22

Results: Specially treated nanoparticles quickly stop bleeding by binding to blood platelets, the core of the body's own clotting system. When injected into rodents in which an artery had been partially severed, the nanoparticles reduced bleeding time from four minutes to two.

Why it matters: Existing methods for stemming blood loss after traumatic injuries work best with open wounds or in the operating room, since they require direct access to

the site of the bleeding. An injectable treatment could effectively stanch internal bleeding from wounds that existing treatments can't reach.

Methods: Each particle contains molecules of polyethylene glycol (PEG)—a water-soluble compound that keeps the particles from sticking to each other or to blood vessels—attached to a polymer core. The PEG molecules are topped with a peptide sequence that binds to activated platelets, helping them stick together to form clots.

Next steps: Researchers plan to test the particles in larger animals, whose circulatory systems more closely approximate those of humans. They will also test them in different types of wounds, such as those that mimic the effects of blast injuries, which are particularly common among troops in Iraq and Afghanistan. The trauma that results from an explosion—for example, when someone is thrown against the ground—can shear blood vessels, causing internal bleeding.

INFORMATION TECHNOLOGY

Securing Web Apps

EXPERIMENTAL SYSTEM WATCHES APPLICATIONS TO MAKE SURE THEY'RE NOT MISBEHAVING ON THE USER'S END

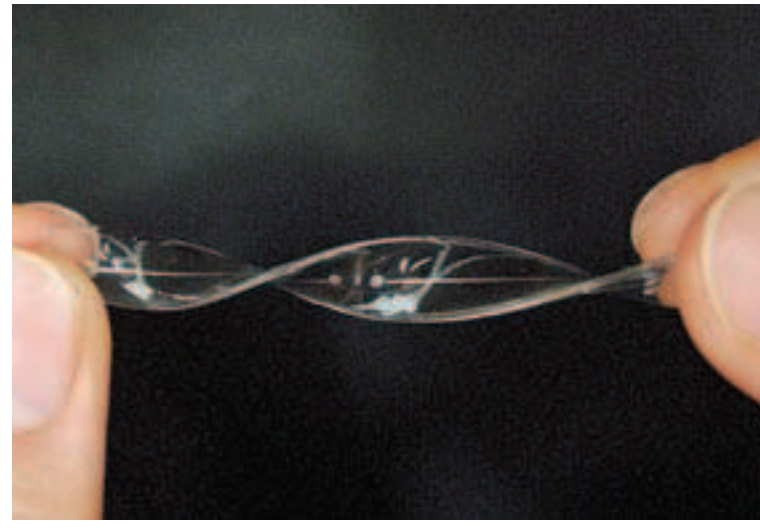
SOURCE: "RIPLEY: AUTOMATICALLY SECURING WEB APPLICATIONS THROUGH REPLICATED EXECUTION"
Krishnaprasad Vikram et al.
ACM Conference on Computer and Communications Security, November 9-13, 2009, Chicago, IL

Results: Researchers designed a system that secures Web applications by protecting against attacks on the portion of the application's code that runs on users' machines rather than on Web servers. They found that the system protected five sample applications, and also a test version of Hotmail, without straining the network, the user's computer, or the server.

Why it matters: The user side of Web applications has been notoriously difficult to defend, because the code on the user's computer can be compromised very easily—even by the user. As a result, some important functions must run on the server, a requirement that slows the system down. For example, an online shopping site could work faster if each user's shopping-cart information and purchase totals were manipulated directly in the browser, but these functions are assigned to the server lest a user hack the system to add fraudulent discounts. The new system would make sure that no such unauthorized behavior occurred.

Methods: The system replicates the part of the application running within the user's browser and runs that replica on the server. Values computed by the replica are compared with those from the real application to ensure that the code is running on the user's machine as it's supposed to; if they don't match, the system disconnects the client, ending the transaction. To avoid overburdening the server's memory and processors, the researchers pared down the cloned software so that it performs only essential actions.

Next steps: The researchers designed their system for applications written with .NET, a software framework that runs on Microsoft Windows. They now hope to see their techniques adapted for applications written using other common programming technologies, such as Silverlight and Flash.



TUNING IN Silvery wires of a liquid-metal alloy, encased in a polymer, form an antenna that still works after being twisted.

Adaptable Antenna

INJECTING LIQUID METAL INTO POLYMER MOLDS PRODUCES EFFICIENT ANTENNAS THAT CAN TWIST AND STRETCH

SOURCE: "REVERSIBLY DEFORMABLE AND MECHANICALLY TUNABLE FLUIDIC ANTENNAS"
Michael D. Dickey et al.
Advanced Functional Materials 19: 3632–3637

Results: Engineers at North Carolina State University created a flexible yet efficient antenna using a liquid metal, a gallium-indium alloy. The antenna is as efficient as a standard copper antenna, transmitting over a broad frequency range at about 90 percent efficiency. It remains functional even when it is twisted, folded, or stretched to 40 percent beyond its normal length.

Why it matters: The antenna could make it easier to send and receive data from flexible electronics, such as sensors incorporated into clothing, electronic paper, or implantable biomedical devices. The radio frequencies it responds to change as it stretches, which means that it could be embedded in machinery or in a concrete structure such as a bridge to monitor it for strain over time.

Methods: The researchers poured liquid polydimethylsiloxane (PDMS) into a mold. Once cured,

NATE DEGRAFF/NC STATE

the PDMS formed a pliable structure with a hollow channel inside. They injected the gallium-indium mixture into the channel and sealed it, creating a simple dipole antenna (like the "rabbit ears" used for analog TV reception).

Next steps: The researchers are building and testing liquid-metal antennas in other shapes, such as the loops, helices, and patches more commonly used in devices like cell phones and GPS transceivers. They are also evaluating other polymers, since PDMS might interfere with the efficiency of these differently shaped antennas.

MATERIALS

Stacked Circuits

MULTILAYERED STRUCTURES BRING CARBON-NANOTUBE PROCESSORS CLOSER TO REALITY

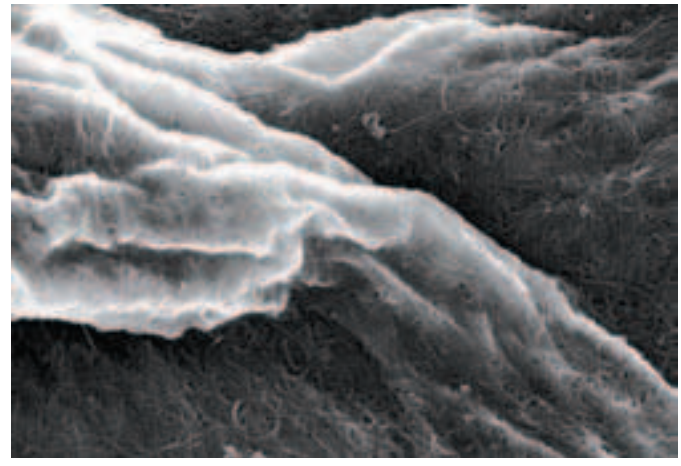
SOURCE: "MONOLITHIC THREE-DIMENSIONAL INTEGRATED CIRCUITS USING CARBON NANOTUBE FETS AND INTERCONNECTS" AND "VMR: VLSI-COMPATIBLE METALLIC CARBON NANOTUBE REMOVAL FOR IMPERFECTION-IMMUNE CASCADED MULTI-STAGE DIGITAL LOGIC CIRCUITS USING CARBON NANOTUBE FETS"
Hai Wei et al. and Nishant Patil et al.
International Electron Devices Meeting, December 6-9, 2009, Baltimore, MD

Results: Researchers at Stanford demonstrated the most advanced computing and storage elements yet made from carbon-nanotube transistors. They also stacked these transistors in three layers, yielding the first multilayered integrated circuits made from carbon nanotubes.

Why it matters: Carbon-nanotube transistors are potentially faster and more energy efficient than their silicon equivalents, but integrating them into complex circuits has been challenging—in part because when researchers grow arrays of nanotubes in the lab, only some of them are the well-formed semiconducting nanotubes that can be used in circuits. Some are defective, and others are metallic, a property that causes circuit malfunctions. The researchers found a way to work around these problems, making the circuits immune to such imperfections. And the techniques allow for multilayered circuits, which can be faster and more efficient than single-layered circuits.

Methods: The researchers grow carbon nanotubes on a quartz substrate at 800 °C and use an adhesive tape to transfer them to a silicon wafer. Then they lay down a special pattern of metal electrodes on top. To eliminate metallic nanotubes, the researchers use the silicon substrate as the back gate to turn off the semiconducting nanotubes; then they burn the rest out with a blast from the electrodes. Next, they use a chemical etching process to remove electrodes not needed for the final chip design. A variant of this technique is repeated to create multiple layers. Layering the circuits is possible because the transfer process can take place at relatively low temperatures (under 130 °C), so the underlying electrodes don't melt.

Next steps: The researchers will work to increase the complexity of the circuits by refining the designs and by developing ways to grow the nanotubes more densely. So far, they have grown five to 10 nanotubes per micrometer; high-performance circuits will require 10 times this density.



POWER PAD Matted carbon nanotubes, shown here in a micrograph, form an energy-storing coating on ordinary paper.

Paper Battery

A DIP IN NANOTUBE INK TURNS OFFICE PAPER INTO AN ELECTRODE

SOURCE: "HIGHLY CONDUCTIVE PAPER FOR ENERGY-STORAGE DEVICES"
Yi Cui et al.
Proceedings of the National Academy of Sciences 106: 21490–21494

Results: Office paper dipped in carbon-nanotube ink becomes a strong, flexible, highly conductive material that can be incorporated into lightweight batteries (where it serves as a conductive layer) or high-energy capacitors called ultracapacitors (where it serves as an electrode). Used in ultracapacitors, the material stored more energy than previous electrode materials.

Why it matters: It's already possible to print lightweight circuits and screens for electronics like e-readers, but conventional batteries still weigh them down. Carbon nanotubes are a promising material because they are strong, conductive, and light, and they can store a large amount of energy—a quality that helps portable electronics run longer between charges.

Methods: Researchers made the ink by mixing carbon nanotubes in water with a surfactant, a chemical that keeps them from clumping together. Paper dipped in this ink soaks up nanotubes like a sponge. After the paper dried, the researchers confirmed the resilience of the material by scratching and rolling it. Then they tested its performance in energy storage devices.

Next steps: The researchers will try to improve the performance of the devices by changing the formulation of the ink. TR

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ICONIC DESIGN
Douglas Aircraft's DC-3, introduced in 1936, was a breakthrough.

The Evolution of Innovation

HOW COMPANIES DEVELOP NEW PRODUCTS AND HOW THE COMPANIES THEMSELVES DEVELOP IN THE PROCESS

By MATT MAHONEY

The companies that the editors of *Technology Review* selected for the TR50 all have strong records of innovation. But how does the innovation process at a startup like Twitter compare with that at IBM? In a series of articles in the 1970s, including a 1978 contribution to *TR*, Harvard business professor William J. Abernathy and MIT professor of management and engineering James M. Utterback posed this basic question:

How does a company's innovation—and its response to innovative ideas—change as the company grows and matures?

Abernathy and Utterback created a model, still in use, that described the life cycle of industrial innovation. They began with two extreme cases to define the limits of their "spectrum of innovators":

Past studies of innovation imply that any innovating unit sees most of its innovations as new products. But that observation masks an essential difference: what is a product innovation by a small, technology-based unit is often the process equipment adopted by a large unit to improve its high-volume production of a standard product.

The authors found that small companies or groups are most often the source of radical product innovations.

New products which require reorientation of corporate goals or production facilities tend to originate outside organizations devoted to a "specific" production system; or, if originated within, to be rejected by them.

A more fluid pattern of product change is associated with the identification of an emerging need or a new way to meet an existing need; it is an entrepreneurial act. ... It is reasonable that the diversity and uncertainty of performance requirements for new products give an advantage in their innovation to small, adaptable organizations with flexible technical approaches and good external communications, and historical evidence supports that hypothesis.

To be sure, radical innovations generate excitement and attract attention, but these are merely the beginning of the story for products that succeed in the marketplace.

One distinctive pattern of technological innovation is evident in the case of established, high-volume products such as incandescent light bulbs, paper, steel, standard chemicals, and internal-combustion engines. ... In all these examples, major systems innovations have been followed by countless minor product and systems improvements, and the latter account for more than half of the total ultimate economic gain due to their much greater number.

Of course, the two extreme cases are just that, and companies like the ones profiled in this issue fall at all places on the spectrum. In fact, the authors argue that successful companies are likely to move from one end to the other in their lifetime. The histories of two very different industries illustrate the common trajectory.

Two types of enterprise can be identified in this early period of the new [semiconductor] industry—established units that came into semiconductors from vested positions in vacuum tube markets, and new entries such as Fairchild Semiconductor, I.B.M., and Texas Instruments, Inc. The established units responded to competition from the newcomers by emphasizing process innovations. Meanwhile, the latter sought entry and strength through product innovation. ... Since 1968, however, the basis of competition in the industry has changed; as costs and productivity have become more important, the rate of major product innovation has decreased, and effective process innovation has become an important factor ... .

*Like the transistor in the electronics industry, [Douglas Aircraft's] DC-3 stands out as a major change in the aircraft and airlines industries. ... Just as the transistor put the electronics industry on a new plateau, so the DC-3 changed the character of innovation in the aircraft industry for the next 15 years. No major innovations were introduced into commercial aircraft design from 1936 until new jet-powered aircraft appeared in the 1950s. Instead, there were simply many refinements to the DC-3 concept—stretching the design and adding appointments; and during the period of these incremental changes airline operating cost per passenger-mile dropped an additional 50 percent.**

The way companies manage this transition from the initial "fluid" phase to the later "specific" stage is vitally important. TR

**For a review of Boeing's new 787 Dreamliner, see "Reinventing the Commercial Jet," p. 80.*

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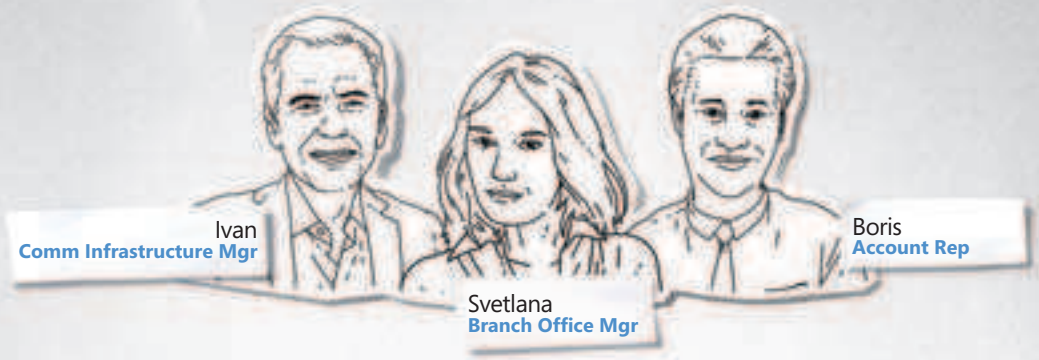

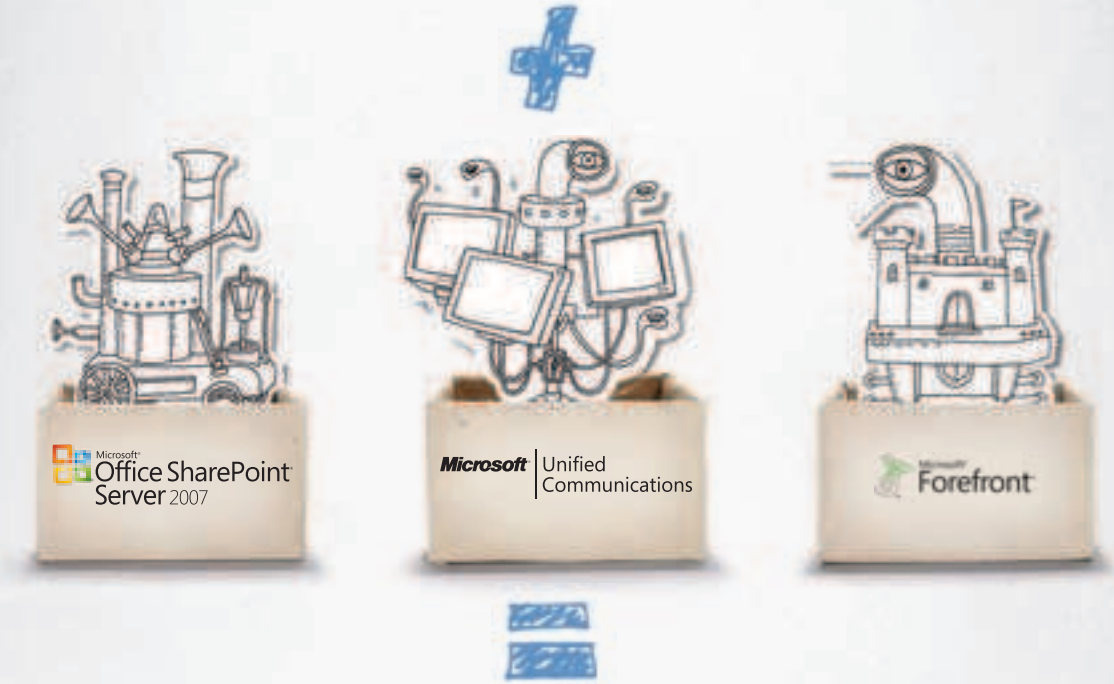

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